

The Factors on which diagnosis in
Smallpox is based

A. F. Cameron, M.A.St.And.

M.B.C.M. Edin. 1896., D.P.H.

Camb. 1901



In London, patients certified to be suffering from Smallpox, are removed to a Receiving Station where they are re-examined. If the diagnosis is confirmed, they are sent to the Hospital. If it is corrected, they are returned home. At the Receiving Station, there are a few beds for doubtful cases.

During the epidemic of 1901-2, 9867 patients were admitted at the Receiving Station, and in 844 of these the diagnosis was corrected. The whole stress of the epidemic fell on the period between August 1901 and July 1902. During this time, I was engaged continuously in dealing with patients, at first, up to November 1901, in the work of treatment in the Hospital and subsequently, to September 1902, in the work of diagnosis at the Receiving Station, in the capacity of Senior Assistant Medical Officer.

The following discussion of the factors on which diagnosis in small-pox is based, is founded on the methods employed at the Receiving Station, and on the personal and critical examination of not fewer than 7000 patients certified to be suffering from the disease.

Among the diseases which most commonly engage the attention of Public Health Authorities in this country, Smallpox is the most important. Its extreme infectivity, making an attack almost certain in the unprotected contact and leading to the rapid epidemic spread of the disease, the high mortality rate, 16.1% in the Hospitals of the Metropolitan Asylums Board in 1901, and the painful character of the disease and its consequences to the individual, are obvious reasons why smallpox holds this position and when present in a community overshadows all other diseases endemic in this country. For these reasons, also, accurate diagnosis in smallpox acquires the greatest importance.

But there are other reasons, arising from the nature of the disease itself, which give diagnosis in smallpox a position which is peculiar. Of no other disease can it be said with more force than of Smallpox that the fate of the individual depends almost entirely upon what may be called the relation between dosage of poison and pre-existing immunity. It is a disease in which the patient under advantageous circumstances, but not necessarily very skilled supervision, is liable to few serious complications and very few sequelae. The issue, in the great majority of fatal cases, is brought about, not by such conditions but

by the continuance of the pathological processes which themselves constitute the disease, so that in smallpox it may be said with considerable truth that the prognosis is established at the onset. Moreover, it can be definitely made in a high percentage of cases within a few days of the beginning of the illness. It is sometimes possible, by vaccination during the first two or at most four days of the incubation period, to avert or at least lessen the severity of the attack, but after that time and certainly subsequently to the onset of the disease we possess no reliable means of modifying its course. If one leave out of account those cases in which the early fatal issue is evidently due to an overwhelming toxæmia, it is generally recognised that the prognosis in smallpox depends on the density of the specific rash; and as Sydenham pointed out particularly on the density of the lesions on the face. Attempts therefore have been made by various means, to control the development of the rash, but as, during the pre-eruptive period, it is impossible to determine what severity the rash will assume, the results of many observations are rendered at least unreliable if not fallacious. Since the issue of an attack of smallpox so greatly depends on conditions already established, and since attempts to influence the course of the disease yield results which are

are so frequently disappointing, it follows that smallpox is a disease which concerns the community more closely than the individual, thus bearing a peculiarly close relationship to preventive medicine, and therefore that diagnosis, as the first step towards isolation and other protective measures acquires an enhanced importance.

If one compare smallpox with some other infectious diseases commonly met with and usually isolated, it is seen that its chief characteristic is the constancy and definiteness of its manifestations.

In Scarlet fever the signs of the disease are often indefinite. Not infrequently and particularly in older children and adults the throat affection is slight and the only evidence of its existence may be simply a faucial injection which is doubtfully morbid. The tongue is not always typical. It may clean in an irregular manner, leaving a surface which does not appear raw on which it is difficult to say whether or not the papillae are more prominent than normal. Above all the rash may be anomalous. Its characteristics are essentially fine distinctions which are very frequently difficult to identify. In the mild cases of the disease, cases which at the present time form the large majority, the rash is often defective in its distribution and faint in its colouring. Very frequently it is evanescent and if its punctate character has not been

well-marked it leaves no trace. In such cases it seems impossible to arrive at any definite conclusion and one may be obliged to depend on the occurrence of desquamation several days later and more or less typical, or on the onset of some complication recognized as frequent in scarlet fever, before venturing any opinion on the condition. On the other hand, there seems good reason to believe that such mild cases, by the development of some mucous discharge even some weeks afterwards, may serve as active agents in spreading the infection.

Similar conditions have to be taken into account in dealing with Diphtheria. Membrane may disappear from the throat but the patient still remain a serious menace to his companions. The diagnosis in the important cases, the cases which are most active in spreading the disease, is frequently settled only by bacteriological examination and negative results must often be disregarded. It is probable that subsequent discharges from throat, nose or ear have similar significance to those following scarlet fever. The patient himself is liable, it may be weeks afterwards, to the onset of severe and often fatal paralysis.

Again, in Enteric fever, the diagnosis is often difficult or even impossible on account of the frequency of variation in the symptoms, and, on occasion, may only be determined by

a process of exclusion. The agglutinative reaction is apt at times to mislead by the introduction of fallacies and even that test is not usually available until several days have elapsed. After convalescence is established, experience shows that for a considerable time, the patient may present a condition closely analogous to the mucous discharge in Scarlet fever, a condition in which, by the presence of virulent bacilli in the urine, he becomes a very potent agent for the spread of infection.

In Scarlet Fever, in Diphtheria and in Enteric fever then it is evident, first, from the standpoint of the community, that the period of provisional diagnosis may be of considerable length, that it is often difficult to determine when a patient ceases to be a source of infection, that the source of infection is very frequently difficult to discover, and may be discovered only by expert and laborious investigation and second, from the standpoint of the individual that complications and sequelae are factors of the greatest importance in the work of controlling these diseases.

Such conditions greatly increase the difficulty of dealing effectively with an epidemic. The source of this difficulty seems to lie in the indefinite character of the signs of these diseases. There is no single feature on which an accurate diagnosis may be based. The diagnosis

in many important cases is made from the co-existence of certain symptoms and signs which by themselves are of little value.

By contrast Smallpox is definite. It is the disease most easily traced, most easily recognized and most easily controlled of those with which the Public Health Authority has to deal. It is a disease in which the doubtful period only exists at the beginning. "It is perhaps of all diseases that in which a certain diagnosis can be arrived at in almost every case". Its incubation period is very constant. Its pre-eruptive stage varies very little in length. Its rash is truly specific. It appears usually after two and certainly in three days from the onset. It consists of gross and therefore very definite elements. It is not evanescent, but passes through a certain well-marked life history by definite stages which require definite times for their accomplishment. From present experience it seems that (a) the most potent source of infection exists in this rash; and it is probable that infectivity not only increases greatly with the appearance and subsequent development of the rash, but also ceases when the last traces of the rash has disappeared.

(a) The most virulent toxæmic cases, though probably more infective, form a small minority of the cases which occur in an epidemic.

It is a remarkable fact that no "return" case of Smallpox has been traced to a patient discharged from the Hospitals of the Metropolitan Asylums Board and this is the more remarkable at a time when the question of "return" cases of infectious disease occupies so prominent a position in the view of Public Health Authorities. There are comparatively few cases in which any complication or sequela, as a possible source of infection, delays the patient's discharge, and the disappearance of the last trace of the rash is the main criterion of the patient's freedom from infection. It is therefore comparatively easy to ascertain when a patient ceases to be a danger to the community and for the same reason the primary source of infection should be easy to discover. It is an accident that smallpox now chiefly affects a class which is nomadic in habit. Examination of suspects in the search for this source requires no appliances and no knowledge beyond the reach of every practitioner.

In small-pox therefore and more especially in cases which from the Public Health point of view are the most important - the mild and ambulant cases - there is one definite sign on which an accurate diagnosis can be based. It is the rash. It appears early in the disease. It persists throughout its entire course. When it has

disappeared it may be safely said that the patient is no longer a source of danger. Throughout its life history, it presents features at every stage which are characteristic and definite.

In this connection it is worthy of remark that, during the London Epidemic of 1901-2, among nearly 10,000 Smallpox patients treated in the Hospitals of the Metropolitan Asylums Board, in no case did relapse occur. Moreover among ⁷²³⁵~~7255~~ patients who were sent to the Hospitals, after revision of the diagnosis at the receiving Stations, between Jan.1st and Dec.31st 1902 only two were found after arrival at the Hospital to be not suffering from Smallpox. Such figures are sufficient proof that diagnosis in smallpox must rest on very definite factors. If one disregard, as one may for the present, those cases of smallpox, in which the virulence of the poison produces a fatal result before the specific rash has had time to appear, since they possess their own peculiar features, and in an epidemic form only a small minority of the cases dealt with, one can say from personal experience, that the factors on which an accurate diagnosis must be based are found in the characters of the specific rash and, in the great majority of cases, in these alone.

The consideration of the other phenomena, subjective

and objective, which may be met with in the disease, justifies this view in shewing that none is invariable in its occurrence.

It is evident, that in very many cases in which an immediate decision is required and especially in those already referred to as the most important from the Public Health point of view, nothing can remain at the time of examination except the rash. Symptoms in such cases must become purely historical. The class most affected by the disease is one which is notoriously unreliable in statement, and this condition is accentuated by the natural resentment to compulsory examination shewn by the suspect who asserts, that he never felt better in his life. On the other hand, in patients who presumably are reliable and desire to be accurate, the occurrence of the classical symptoms is often difficult to elicit even by leading question. A partial immunity shews its influence chiefly in the life history of the specific rash, but it also affects the pre-eruptive stage of the disease.

To obtain a clear history of the occurrence of a sudden onset of severe pain in the back, head and limbs, with repeated shiverings and vomiting is of value, no doubt, as indicating the beginning of some acute and probably infectious disease. It does not necessarily

point to Smallpox. Of the other initial symptoms various

Of the symptoms which are associated with the pre-eruptive stage of the disease, the sudden onset, pain in the head and perhaps vomiting are the most constant. The occurrence of pain in the back seems to have received a position of undue importance. Certainly severe lumbar or lumbosacral pain does not occur with the invariability on which so much stress is laid. Even in trustworthy patients, presenting attacks of moderate severity, in which the lesions at full development may number between one and two hundred on the face, the back-ache may have been so slight that it is quite forgotten. The situation of this pain seems as variable as its severity. Often it is felt in the dorsal region. Many affirm that all the pain they suffered was in the neck and amounted to no more than a slight stiffness. On the other hand some, in whom the onset is exceedingly severe, refer the pain entirely to the front of the body. Some describe it as a sense of tightness or suffocation in the chest, others as severe abdominal pain which they mistake for colic. In the latter the flinching caused by superficial palpation and the aggravation of the pain on deep inspiration and sudden movement, seem to indicate that it is really referred to the abdominal wall, deep palpation producing no increase either in resistance or discomfort.

The severity of the other initial symptoms varies in a similar way. There may be repeated rigors or only a shivering. Vomiting is frequent but some patients complain only of nausea.

What then is the value in diagnosis of these subjective phenomena ? With such symptoms the diagnosis may be smallpox. It may equally well be Influenza. It very frequently is. The only indication they afford is the necessity of making a careful examination of the skin as well as of other organs. The patient frequently comes under observation for the first time, at the end of one or two days illness. The pain and sickness having abated, he seeks advice to prevent its recurrence. An early and discrete smallpox rash is easily missed, if a careful examination of the skin is not made.

But, even if of considerable severity, such symptoms do not necessarily mean Smallpox. Two patients from the same house, where they occupied adjoining beds, were certified to be suffering from smallpox. On arrival at the receiving station one had a confluent vesicular rash. The other had lobar pneumonia. The lower and middle lobes of his right lung were in the stage of consolidation. His face, his eruption of herpes, his breathing all pointed to the condition. Fortunately the vaccination

was successful and he did not contract the disease. His illness had a sudden onset with chill, pain in the head and back, and sickness.

The presumption in favour of Smallpox becomes stronger if a reliable history of contact with the disease is obtained. But the indiscriminate certification of Contacts with febrile symptoms is fruitful of many mistakes. Between August 1st 1901 and November 21st 1902, 197 patients were sent to the receiving Stations, certified to be suffering from Smallpox, presumably on account of a more or less characteristic onset since they shewed no rash. Of these 55 developed the rash subsequent to admission, while in 142 the symptoms either passed off or some other disease declared itself. When notification is immediately followed by removal to Hospital as in London, such patients are exposed to the risk involved in a detention for varying periods in the neighbourhood of virulent Smallpox. If vaccination is successful they are safe. But one has to consider the possibility of meeting, especially in epidemic times, with some inactive strains of lymph.

On the other hand, the failure to recognise the possibility of symptoms being due to Smallpox is incomparably more important than this risk to the individual. Intelligence of mistakes in this direction was frequent

throughout the epidemic. The law does not recognise the existence of contacts or suspects, so that in many cases of doubt certification is the preferable course.

The question of the value to be attached to symptoms as a guide to diagnosis in Smallpox acquires additional importance in view of the possibility of the occurrence of Smallpox without eruption. By this one does not mean the fulminant type of the disease, the cases which are so rapidly fatal that the specific rash has not time to appear. Such cases have, as their characteristic clinical feature, visible haemorrhage, evident during the whole course of the attack or breaking out suddenly just prior to the fatal termination. On the other hand, the type which has been styled Variola sine eruptione, if it occurs, has its place at the opposite pole in degree of severity. The importance of cases of this type depends altogether on their invariably favourable course and termination, increased opportunity being given thereby to any infectivity they possess. The disease progresses no further than the pre-eruptive stage. The patient recovers and no specific rash develops. It is clear that the only cases in which the question of smallpox without eruption is likely to arise must be those in which contact is definitely ascertained and which, at some time within the possible incubation period, develop the

Station, by kind permission of Mr. Stanley, Medical Superintendent.

symptoms of the onset of an acute febrile disease. In most instances probably these symptoms will not be severe. 8 days before admission.

The strongest argument in favour of the occurrence of this type of the disease, rests on the fact that the influence of a partial immunity is exhibited in the eruption but not always in the pre-eruptive stage and that its effect, in part, is to render the rash more discrete. In the present state of our knowledge of the actual contagium of smallpox, definite settlement of the question does not seem possible, but one may make the following statements based on the experience of the London epidemic of 1901-02. ^{*} Of the patients admitted during 1902, 65 had no skin lesions on admission, and were returned home from the receiving station when their symptoms had passed off and no specific rash had developed. Of these 57 had a history of contact with the disease. In 63 revaccination at the receiving station, i.e. subsequent to the onset of their illness, was successful. Of those in which the operation was unsuccessful, the following are the particulars of their state as to vaccination and other notes bearing on the question.

^{*} Compiled from the records at South Wharf Receiving Station, by kind permission of Dr. Wanklyn, Medical Superintendent.

D.H. Age 9. Successfully vaccinated in infancy, was a contact and was said to have had headache and vomiting 9 days before admission.

M.A.B. Age 69. Successfully vaccinated in infancy, was a contact, and gave an indefinite history of illness about three weeks before admission. Possibly she may have had a very discrete rash of which all trace had disappeared.

In no case was the occurrence of suggestive symptoms backed by the subsequent appearance of a rash, of the type of any primary rash of Smallpox. Enquiries were systematically made at the receiving Station and by the Ambulance Nurses for the purpose of tracing the source of infection, but in no instance was evidence forthcoming of the existence of previous cases of this description. If they had been frequent some instances would have come to light, and therefore the conclusion seems justifiable that variola sine eruptione is at least a rarity and if it does occur, that its infectivity is very slight.

There are certain objective conditions, comprised under the head of general aspect of the patient, which, though not possessing the invariability and definiteness of the specific rash, are yet in some cases of value as indicators. Taken together they form a mental picture which, when subjected to the necessary test of a critical



The expressionless face of the Smallpox patient.

examination of the rash, is often found to be reliable. They are of value in those cases in which the diagnosis is rendered uncertain on account of the early stage at which the patient comes under observation. Their occurrence, practically, is limited to such cases. Typically the patient presents an appearance of complete prostration. Particularly towards the end of the pre-eruptive stage, he [has the general aspect of one who has passed through a long and exhausting struggle. His face has lost its expression. The lines have partly disappeared. As it has been expressed, his face is mask-like and there is a want of tone in all the muscles. When he speaks this condition becomes more apparent. He speaks with evident effort and his voice is low and monotonous. He is listless and indifferent to his surroundings, though his eyes may be clear and bright. The question as to the disease from which he suffers has little interest for him. The greater the physical development the more marked in this condition. The mental attitude is similar. There is loss of tension, shewing itself in a lengthening of the reaction time and a defective control. When a question is put the answer is appreciably delayed. A request to shew his tongue or to put out his hand often

✓
"Variola and Varicella. Differential diagnosis", by W. M'C. Wanklyn, M.R.C.S., L.R.C.P., Medical Supt. Smallpox Receiving Stations of the M.A.B. British Medical Journal July 5th 1902.

requires to be repeated. Such movements are often retarded, and tremulous or even jerky in their performance. It is evident that their completion gives relief. The patient staggers in his walk and tends to fall if not supported. Frequently he volunteers the statement that he feels much better and will soon be all right. Such is the typical condition. The more severe the attack the more striking is the picture. In the most fulminant case the aspect of the patient resembles that of one suffering from severe shock and loss of blood. His face is drawn and pallid. His respiration is sighing or even gasping. He tosses himself about continually and cries out at frequent intervals. His attention is fixed with difficulty and he complains only of agonising pain, now in his chest then in his back, his head or abdomen. In other less fulminant but equally fatal cases, the facial expression is masked at first by the general vivid erythema and later by the numerous haemorrhages and increasing turgescence of the skin.

These conditions are associated with the onset and pre-eruptive stage. They vary in severity with the severity of the initial symptoms. If the rash which subsequently develops is mild and discrete they tend to subside rapidly but may persist for a day or two after the rash has appeared. In the more confluent and less

modified cases the facial expression becomes obliterated as the rash develops. If the case is mild all through its course these conditions are not marked and in very few cases do they persist beyond the fourth day of the illness. They are not to be regarded as essentially peculiar to Smallpox but only as probably more frequent in their occurrence and more intense in their manifestations in that disease than in others of its class. In cases where they are present in a marked degree, and associated with symptoms and a definite history of contact the diagnosis of Smallpox will be correct in a large percentage.

The temperature in Smallpox seems to bear slight relation to the severity of the attack. At the onset and during the pre-eruptive stage it may rise no further than 101° F. to 102° F. or it may reach 104° F. to 106° F. In many of the most rapidly fatal cases it rises no higher than 100° F. to 101° F. In all very mild cases there is no secondary fever. In many even of those which shew a rash of moderate severity numbering say between 200 and 300 lesions on the face the secondary fever may be very slight and if modification is well marked probably will not occur. It follows that in the very cases in

* A similar condition is said to occur in Plague.

which diagnosis is called for the thermometer can afford no assistance, since the absence of fever in pathological skin conditions is not a point of differential value.

On the other hand, in those cases in which one has opportunity for observation throughout the pre-eruptive stage, a remission or intermission occurring during the third day, simultaneously with or just subsequently to an eruption of "spots", however discrete the eruption is, must be regarded as an indicator of very considerable importance.

The detailed examination of the various systems, with the exception of the skin conditions, affords as little assistance in diagnosis in Smallpox as in other diseases of its class. In the early stages the tongue becomes covered with a thick white fur not only on the dorsum but ^{frequently} also on the sides and under surface. This fur, in severe attacks and particularly in virulent and rapidly fatal cases, invades the entire buccal mucosa, giving a uniform greyish white appearance to the surface which has been compared to diphtheritic membrane. Early in the eruptive stage lesions appear on the soft and hard palate, on the mucous membrane of the cheeks and on the tongue. The invasion of these parts seems to have this order of frequency. These lesions appear as small spots of a deeper red than the surrounding mucosa and have a

glistening surface. They are not so uniformly circular as the lesions on the skin. They develop rapidly and are usually vesicular in twenty-four hours, appearing as flat white spots very slightly raised above the surrounding surface, with a sharply defined edge, where the pellicle is attached, and a narrow dark red areola. This stage of the lesion is very short and most frequently at the time of observation, the vesicle has already ruptured, producing an ulcer very slightly depressed, with the remains of the white pellicle adherent to its edge. The number of the lesions on the mucous membrane is proportionate to the density of the skin rash. In severe cases they assist greatly in producing the uniform diphtheritic-like covering of the mucous membrane. In the mild and modified attack they partake in the shortening of the life history which is evident in the skin rash.

The occurrence of these lesions is a point of considerable diagnostic ^{the} value in the examination of an early rash. They are present in a very large proportion of cases. They are earlier in their appearance than the lesions on the skin. But they are much more rapid in their development, are the fewer in number the more discrete the rash, and ^{frequently} ~~usually~~ have disappeared by the time those on the skin have become fully vesicular. Their value then is limited to the earlier stages.

The result of the examination of the Circulatory and Respiratory Systems is usually negative. In severe cases in the later stages, especially in children and infants, the voice is hoarse and aegophonic in character. There may be complete aphonia. Conditions frequently to be observed in the examination of the nervous system have already been described. Retention of urine may occur in severe cases. The significance of purpuric conditions which occur in such cases is considered later.

There are some practical details which, though important for an efficient examination of any skin condition, become of cardinal importance when Smallpox is a possibility. Experience has shewn how easily neglect of these details leads to error. The first essential is a good light. Daylight is of course the most satisfactory. It is probable that the want of a sufficient light so much experienced in London during the season of fog, is responsible for many mistakes in diagnosis. This difficulty is accentuated by the conditions existing in the houses of those whom Smallpox most affects. In such circumstances it is advisable to take some trouble to obtain the best artificial light available, for, even when working with a 16 candle power electric lamp, an early measles often seems remarkably like an early smallpox rash.

Another point, the importance of which cannot be too strongly emphasised and will be more evident in dealing with the characteristics of the specific rash, is the necessity of making a complete examination of the skin. If possible the patient should be stripped, so as to bring face, chest, arms, hands, legs and feet simultaneously under view. Thus one gains a general idea of any rash which is present. With the exercise of ordinary care for the feelings of the patient, and an explanation of the importance of the proceeding from the point of view of diagnosis, one very rarely experiences any difficulty in carrying out this practice. The bird's eye view thus obtained is of the greatest value and alone is sufficient in many cases to exclude smallpox. The want of it is a fruitful source of error.

Considering the class of patient which Smallpox most frequently affects, it is natural that the use of soap and water becomes an important aid in diagnosis. It is often a necessity in the early stage of the rash, when, without a preliminary cleansing, the tiny macules and papules will remain hidden. This is the case also at a late stage in very discrete attacks, when the lesions on the face and trunk are few and not sufficiently definite for a positive diagnosis. In many of the latter class, the lesions on the hands and feet alone

are those which shew characteristic features and their presence even is often missed on account of the covering of foreign matter. Again, in the examination of contacts and in the search for a primary source of infection, one expects to discover a rash probably at a late stage of its development. The patient may shew no lesions on the face or trunk. He may have forgotten or may deny any recent illness. The only trace of the disease may be found on the palms of the hands and soles of the feet, and for want of soap and water the characteristic crusts will often remain hidden, even in individuals who are comparatively cleanly in their habits.

A hand lens will be found of considerable assistance especially in the examination of early rashes. It often shews characteristic appearances in macules which seem at least indefinite to the unaided eye.

The value in diagnosis of an observation of any scars of vaccination shewn by the patient is very limited. Recent and successful vaccination means immunity. The immunity conferred by a primary vaccination gradually and completely disappears. Virulent Smallpox occurs very frequently in adults who show scars of vaccination in infancy. Its effective period varies with the efficiency of the operation. No doubt individual idiosyncrasy also must be taken into account. But it

is impossible in most cases to form any judgment as to the degree of the immunity possessed by the patient, and in others the deductions to be drawn are at best only probabilities.

Successful vaccination leaves a scar, the surface of which is foveated in varying proportion. The following figures seem to shew that in the cases in which a certain immunity still exists as a result of a primary vaccination, the immunity is more closely related to the extent of the foveated area than to the number of scars or to the total area of scar tissue.

Among 1763 patients admitted to the Hospitals of the Metropolitan Asylums Board during 1901, there (a) were no vaccinated children under the age of 3 years. Between the ages of 3 and 7 years there were 6. Between the ages of 7 and 10 years there were 14. Between 10 and 15 there were 69 and between 15 and 30 there were 626.

Compiled from Statistics of Vaccination in Annual Report of Metropolitan Asylums Board for 1901.

(a) Successful primary vaccination during the incubation period is not included.

Patients who shewed Scars of primary

Vaccination.

Total area of Scars.

	Half a sq. in. & over.	Between $\frac{1}{3}$ and $\frac{1}{2}$ sq.in.	Less than $\frac{1}{3}$ sq.in.
Under 10 years	13	2	5
Between 10 & 15 years	49	9	11
" 15 " 30 "	539	46	51

Extent of Foveated Scar.

	$\frac{1}{2}$ sq.in. & over.	less than $\frac{1}{2}$ sq.in.	Plain Scars.
Under 10 years	3	7	10
Between 10 & 15 years	11	30	28
" 15 " 30 "	150	278	198

Number of Scars.

	<u>Four</u>	<u>Three</u>	<u>Two</u>	<u>One.</u>
Under 10 years	11	4	1	4
Between 10 & 15 years	42	9	8	10
" 15 " 30 "	306	152	104	64

The only conclusions one may draw from these figures are :-

1. That a well vaccinated child under 7 is not likely to be suffering from Smallpox.
2. That it is unsafe after the age of 7 to lay any stress on the presence of scars of an operation performed in infancy.
3. That foveated area of scar is more reliable evidence of immunity than either total area or number of scars.

On what grounds can an opinion as to the age of the scar be based ? From observation of the Scar after it has reached a certain age it is impossible to say how long a time has elapsed since the operation was performed. For a time the scar is pigmented. It gradually loses this pigment and at length becomes white and when this stage is reached, a scar which is 5 years old does not differ from one which is 30. Therefore, except in the case of children, one can say that a scar is evidence of recent vaccination only as long as it remains pigmented, and that the presence of pigmented and foveated vaccination scars as negative evidence is of some weight in diagnosis, indicating that the vaccination has been both recent and successful. But in practice this stage of pigmentation is the only one in which an observation of the results of vaccination has an appreciable clinical value. During the period preceding the fall of the scab its value is very small. Such as it is, it increases as the age of the lesions produced by the operation exceeds the age of the suspected rash. Smallpox and Vaccinia can coexist. Vaccination performed at the very end of the incubation period is frequently successful and Smallpox has occurred certainly as late as the 10th day of successful vaccination.

x Metropolitan Asylums Board Report for 1901. Report on Vaccination of Patients by T.F.Ricketts, M.D., Medical Superintendent Smallpox Hospitals.

In addition to the specific rash there are other conditions to be observed in the skin in Smallpox. The different forms of "initial" rashes which occur hold a position of considerable importance in the diagnosis of the disease. But their occurrence is not constant and in the majority of cases they are evanescent. In many of the cases in which a diagnosis has to be made, no such condition may have been present, or if it has been present it has disappeared by the time the patient comes under observation. In contrast with the papular rash they are not truly specific. Their persistence and their value in diagnosis vary directly with their intensity, so that certain types afford in themselves almost a sufficient basis for a positive diagnosis. But, on the other hand, there is no type which may not be simulated, and sometimes very closely, in other conditions, so that considerable discrimination is required in the estimation of their clinical value. The term "initial" as applied to these conditions does not mean that the rash is limited in its occurrence to the initial stage of the disease, nor that it necessarily appears at the onset of the illness. These rashes may occur at any time during the pre-eruptive period, and may persist for one or two days after the specific rash

has appeared. The term "primary" seems to be more in accordance with the time of their occurrence and to express more clearly their true position as manifestations of the disease. The term "accidental" ^(a) as used by one writer seems altogether a misnomer.

^(b)
As Curschmann has pointed out these rashes are of two main types :- Erythematous and Haemorrhagic.

Both forms may be seen at the same time in one patient. In some cases there is a mingling of the two forms, petechiae occurring on an area of erythema. In other cases the two remain almost quite separate, affecting different areas of the Skin. For example the patient may shew a simple erythema on forearm and thorax and groups of petechiae in the flexures of the elbows, round the armpits and along the folds of the groins.

The Erythematous primary rash of Smallpox varies very widely in its extent and intensity, but it always remains a simple erythema except in the cases already mentioned. Generally speaking its tendency is to occur in patches of irregular shape and, although in certain cases it seems to aim at symmetry, it is more frequently

(a) "Variola and Vaccinia" by Sir J.W. Moore in "Textbook of Medicine" Ed. by G.A. Gibson, M.D. etc.

(b) "Smallpox" in ^{see} Ziemssen's Cyclopaedia Vol.ii.

distributed in an irregular and asymmetrical manner. The fainter its colouring, the more irregular is its distribution and the more evanescent is its character. Usually also its colouring varies with the size of its patches. It has a tendency to fade from one part and appear in another. The areas of erythema are not raised above the general surface. One finds it impossible in passing the finger over the skin to perceive when the margin of an area of erythema is reached. The rash, in my experience, is never urticarial in character. It fades on pressure. When pressure is removed it reappears as a blush rapidly deepening in colour over the whole surface. It does not reappear at several points on the surface to which pressure has been applied.

It is convenient for purposes of clinical description to subdivide the erythematous rash into two varieties. But the sub-division is based on one or two features only and the one variety is not distinctly marked off from the other. In practice both are not infrequently present in the same case.

To one variety of the rash which shews small patches of erythema, usually a faint red or pink in colour, and often only evident as a mottling of the surface, the term "morbilliform" has been applied. The reasons for



Third day of disease, shewing primary erythematous rash. Here and there are lesions with broad areolae. The erythema does not stand out well in the photograph since it is not raised.

Measles. The rash is raised and therefore stands out well in the photograph. Contrast with No.

giving it this name are not very obvious. The only feature which Morbilli and this form of the erythematous rash of Smallpox possess in common seems to be the faint red or pink colour. The patches of erythema are not raised. Their arrangement only very roughly can be called crescentic. In size, they are several times as large as those of measles. The marbled condition of skin seen in some patients, in whom this rash is very slightly evident, resembles to a certain extent the condition in measles when the rash has faded almost completely, but the whole pattern is of much larger design. If one except the intense and general form of the rash which makes an early appearance in many of the most virulent cases of the disease, it is very rarely indeed that the erythematous rash affects the face. This variety shews the migratory tendency well. It may be present at one time on the chest and back and in a few hours shew itself on the forearm when that on the trunk has almost disappeared. Frequently it seems to advance over the surface, fading away gradually at the other extremity of the affected area. In some cases it affects very large areas. It presents the appearance of a network, with strand as broad or broader than its mesh which is of varying size and irregular outline. It may be described as a reticulate erythema.

The other variety is more intense in its colouring and more definite in its other characters. It shows a tendency to symmetry in its distribution. The patches are larger than those of the former type and their outlines are often well defined. Except for the fact that it is not raised and does not shew the characteristic advancing margin, it presents a superficial resemblance to erysipelas. When it invades the greater part of trunk and limbs its appearance on inspection is not unlike that of an intense Scarlet Fever rash. Though it may be found on any part of the body it has certain sites of election. It frequently affects the inner side of the foot, and the skin over the metatarsal and phalanges of the great toe, the radial aspect of the lower half of the forearm, the extensor surfaces of the limbs. Frequently it covers the joints and may be limited to these parts. The elbows, the knees and the shoulders most often shew the condition. If symmetrical the one side usually shews very much smaller areas than the other. In colour the patches are a bright red. On the trunk or limbs a papule is sometimes seen surrounded by a broad band of vivid erythema.

The value in diagnosis of the erythematous rash depends on its distribution. The limitation to certain parts of the extensor surfaces of the feet and hands,

the involvement particularly, of the larger joints, the well marked margin in the second variety, with an area of skin beyond it which seems quite normal, and, above all, the fact that the face is very rarely affected when the rash is not general over the rest of the surface, are points of some value. Its value also depends on its colour. The brilliant red shewn in some cases is most striking and should be suggestive. The other general characters already mentioned must also be taken into account. What has been described as the reticulated erythema is important, if its features are properly appreciated and especially if there is opportunity of observing its migratory tendency. But to expect to meet a primary rash of Smallpox which resembles measles will be fruitful of error. The occurrence of papules surrounded by areas of a brilliant erythema is an observation of the greatest import.

As has been pointed out, the Erythematous rash may affect large areas of skin so that, in what may be called its confluence, it may vary from a condition shewing a few patches on the arms or trunk, to a condition in which the whole surface of the trunk and limbs is involved. It is only in cases of the latter class, in my experience, that the face is affected.

Clinically, the cases in which these conditions are approximated, form the connecting link between the erythematous rash and the early stage of one type of virulent Smallpox, in which, very soon after the onset, usually within a few hours, a brilliant erythema appears and covers the entire surface, involving the face equally with the rest of the trunk. With an onset which is usually of considerable severity, the occurrence of this universal rash of brilliant scarlet colour, more intense and more evenly distributed than Scarlet fever, is rarely to be mistaken. At the beginning it is a simple erythema which fades completely on pressure. But very soon a change occurs. In many cases so rapidly does it take place, that it seems almost perceptible from one minute to another. The colour becomes more and more dusky and haemorrhages shew themselves. Usually these appear first in the regions of the groin and flank. They may be masked at the time of their onset by the general rash, but they are evident when pressure is applied. The subsequent development of these cases is considered later.

Very rarely, occurring in one case in my experience in the epidemic of 1901-2, the erythematous rash has a distribution closely corresponding to the common

distribution of the petechial primary rash. The patient in whom this condition was noted developed haemorrhages generally, while the erythema lost in colour and faded leaving some staining. Later, he presented all the features of the intense toxæmia, to which he rapidly succumbed.

Therefore, not only may the Erythematous and Haemorrhagic rashes coexist, almost from the onset, but in many rapidly fatal cases the precursor of the other malignant manifestation is an erythema of general distribution and great intensity.

For the purposes of clinical description it is best to consider the haemorrhagic primary rash along with other purpuric manifestations of the disease. In Smallpox there is a peculiar liability to blood extravasation. This liability is greatest in the eruptive stage. It seems to increase up to the period of the appearance of the true rash and then to decline rapidly as the rash develops. Most frequently this condition takes the form of cutaneous, Sub-cutaneous or Submucous ecchymoses, but it may also occur as actual bleeding from mucous surfaces and internal organs. The latter form except perhaps in some cases of menorrhagia, carries with it the gravest prognosis. The same is not true of certain forms of haemorrhage

into the skin. They occur in a comparatively large proportion of cases. When the graver condition is present they are very rarely, if ever, absent. Being more frequent and more easily noted they are of greater value in diagnosis. An examination of the records of 1232 consecutive cases admitted to the Hospitals during 1901 shews that Skin haemorrhages occurred at some time in the course of the attack in 271, and that in 70 of these the presence of the more serious condition was also noted. It is probable that this percentage 22% would have been increased if opportunity had been given for observing the earlier stages of many of the mild cases admitted at a late period of the disease.

Skin haemorrhage in smallpox may occur at any time from the onset of the disease to the time when desiccation of the pustules begins. From the point of view of diagnosis, the appearance of the true rash naturally divides this period into two stages. The haemorrhages vary greatly in size. They occur in all grades from minute petechiae to spots $\frac{1}{8}$ to $\frac{1}{2}$ inch in diameter. There may be large necrotic-like patches formed by the coalescence of small areas of haemorrhage. The colour of the lesions depends on the volume of blood they contain and on their depth in the skin.

The small petechiae are bright red, while the larger spots are purple, violet or even black. The latter have been well described as "inkspots".[‡] The bluish white, bruise like, subcutaneous haemorrhage is not frequent in Smallpox. In outline haemorrhages which have an appreciable area are usually regular and tend to be circular. From their formation the larger patches have a less regular margin.

Any grade of skin haemorrhage may occur during the pre-eruptive period and clinically any haemorrhage occurring in this period may be styled a haemorrhagic primary rash. It may be apparent very soon after the onset or suddenly burst out a few hours before death. The persistence of a haemorrhagic focus depends on the amount of blood it contains. So that the purple petechiae and the larger lesions persist longer than the smaller red petechiae which soon fade and disappear. The larger the individual focus and the more numerous the larger foci are, the graver is the prognosis. Usually these large purple lesions are seen scattered over the surface, affecting head, trunk and limbs. They do not seem to have any tendency towards a definite distribution. Generally speaking they are later in their appearance than the smaller red and purple petechiae. The

[‡] "Smallpox" J. MacCombie, M.D., "System of Medicine" Vol. ii. Ed. by Clifford Allbutt, M.D., F.R.C.P., &c.



Haemorrhagic primary rash of moderate intensity.



Third day of the disease. Moderately severe groin rash.

latter, though they may be seen irregularly scattered, have a tendency to occur in clusters. They particularly affect the flexures. Except in the most virulent cases, they do not appear on the face. They exhibit a very marked preference for the groin, just below the line of Poupart's ligament. In that situation a petechial rash is often seen when the rest of the skin shews no trace of haemorrhage. The localised character, the density of the setting and the variegated appearance produced by the different colours of the petechiae are very striking. This groin rash occurs in all degrees of intensity. There may be a few scattered petechiae or a mass of lesions so densely set, that it is difficult to place a pin's head on unaffected skin within the area they cover. Usually both sides are affected but not to an equal extent. Typically, the lower border of the area involved is sharply defined and extends as a nearly straight line across the thigh, almost parallel to, and two to three fingers breadth below Poupart's ligament. The density of the rash decreases as it passes on to the abdominal wall and a band of petechiae crosses the lower abdominal regions from one groin to the other. This band may be broad enough to extend above the umbilicus but it rarely does so, and the rash as it passes up towards the umbilicus thins out gradually so



Fourth day of disease, shewing severe primary
haemorrhagic rash in the groins and axillae.
The papular rash is seen on the face and legs.

that the upper margin is ill-defined and irregular. The rash which has this typical distribution has been compared to an inverted triangle. The sides which meet to form the apex are straight but the base is irregularly curved and passes outwards and upwards from the middle line towards the flank, where the petechiae are usually few in number and always more scattered. Next in frequency to the groin the rash is found in the corresponding position at the upper extremity. In a few rare cases the axillae shew a dense rash while the groins are almost free but usually the involvement of the axilla increases with the density of the groin rash. On the flanks, between the crest of the ilium and the level of the lower angle of the scapula, there are usually only a few scattered petechiae. Often this area is entirely free. Passing upwards to the armpit the density rapidly increases and the rash involves both outer and inner walls. It avoids the apex of the cavity. Scattered petechiae extend inwards over the pectoral muscles and below the clavicle. If the rash is intense it can be seen both from in front and behind when the arm is close to the side. In such cases also a band of scattered petechiae may be seen crossing the back about the level of the crest of the ilium. In one case a collar of petechiae was noted encircling the neck.



Third day of disease, shewing densely set haemorrhages.

This petechial haemorrhage makes its appearance usually within twenty four hours of the onset. In certain cases, - those in which the petechiae are of moderate density and limited distribution, - the rash fades as the true rash develops and in two or three days its position is occupied by a brown staining which afterwards completely disappears. In others, although the smaller petechiae fade, fresh haemorrhages of the larger size make their appearance and rapidly increase in number. Usually they are scattered irregularly over the surface of the body. Often they are numerous on the forehead and scalp. They appear on the eyelids. Haemorrhage occurs under the ocular conjunctiva, commencing at either canthus, and spreading rapidly, so as to cover the sclerotic completely and cause the cornea to appear depressed in its dark red setting. Blood may ooze from the eyes, from the gums and from the lips. Active bleeding may take place from any orifice.

This virulent type of Smallpox is usually ushered in by an onset of exceptional severity. As has been pointed out, its earliest manifestation may be an intense and general erythema appearing with or very soon after the onset.

But there are some cases, rare, but of considerable significance in which the skin may remain perfectly

clear, up to a few hours before death. One such case was noted during the epidemic of 1901-1902 :-

E.H. female, age 21, admitted at the receiving Station in the afternoon of Dec. 6th 1901, was a contact and gave a history of a typical onset of great severity on the morning of the same day. The pain was continuous, and was felt in the back and in the abdomen. Headache was severe and vomiting frequent. She was at the third month of pregnancy. On examination there was no eruption and no haemorrhages in the skin, but her facial expression and general condition were suggestive and along with the history of contact were almost sufficient. She appeared most acutely ill. Her pallor was marked. Her breathing was rapid and at times gasping. The temperature ^{was} ~~of~~ 101° F. The only other positive fact ascertained by physical examination was that abortion threatened. The bleeding was very slight. The usual palliative treatment was adopted, and, except for the appearance of suffusion of the eyes, her condition remained the same until the afternoon of the following day when abortion took place. Haemorrhage was severe but was checked. Subsequently the pain did not abate. Late on the same day, purpuric spots appeared on the eyelids, on the abdomen and lower part of the back. Subconjunctival haemorrhage rapidly



Third day of disease, shewing thickly set haemorrhages
of the rapidly fatal case.

spread. There was a constant cough and the sputum was deeply tinged. Death took place shortly before six o'clock on the following morning, Decr. 8th, eight or nine hours after the first appearance of the skin haemorrhages and less than forty eight hours from the beginning of the illness. There was no trace of any papular rash.

Such was the most rapidly fatal case which occurred to our knowledge during the epidemic. Of the still more fulminant cases described as terminating in a few hours with no appearance of any purpuric condition, but, in which, post mortem, large internal haemorrhages are found, no instance was recorded. Such cases must be very rare.

It is more usual, especially in those in which the onset is marked by the general erythema, for death to occur three to five days from the beginning of the illness. For the first twenty-four to thirty-six hours the features of the patient, except for the presence of the erythematous and purpuric rash, are not much changed. On palpation one can detect little difference from the normal skin. But as time goes on a change in his aspect becomes more and more marked. An increasing turgescence appears. The skin, particularly of the face, forearms, hands and feet becomes swollen. On the



Third day of disease shewing the commencing turgescence
in the virulent toxæmic attack.

face this swelling is most evident on the forehead. There the skin is felt to be thickened and less easily moved than is normal. By palpation one can recognise that the surface is composed of minute and very closely set irregularities. At a later stage, the sensation has been well compared to that obtained in passing the finger over dressed leather or pigskin. On the backs of the hands and forearms the irregularities are more easily perceived. The surface may feel as if wrinkled, while the skin of the palms and soles and of the pulp of the fingers and toes is tense, often very tender, has a dull grey colour and may even give a false idea of fluctuation.

This change is brought about by the rise of the papular rash. But the papules are so "closely set, the one against the other,"[‡] that individual lesions are not perceptible, at least on the face, and often just perceptible on the hands and arms. It is rare for cases of this type to pass beyond this stage; but in a few, life is prolonged and further development of the rash takes place. Confluent vesiculation occurs, resulting in the formation of large, flat blebs on the face, and

‡ "Lectures on Diseases of the Skin", Lecture XIV. on "Variola" by Moritz Kaposi.

extremities and to a less extent on the trunk. In one patient whose illness lasted for eight days and who shewed a considerable number of the larger type of skin haemorrhages such confluent vesiculation occurred. The blebs were filled with blood-stained serum. The pellicle of many was torn by the continuous tossing and scratching of the patient in his delirium. The condition of his back, arms and legs just before death, closely resembled the last stage of acute exfoliative dermatitis.

Such cases, in which the later aspect of the patient is referable to the presence of the true rash, form the great majority of those in which skin haemorrhages are met with in the second stage of the disease. That is to say the haemorrhage of the second stage is usually a continuance, often in increasing severity of a condition which has appeared soon after the onset. It is not frequent as a fresh manifestation after the papules are fully formed and still less frequent after the rash has reached the vesicular stage. But there is a form of skin haemorrhage which can occur only in the second stage. It is closely associated with the true rash. It may occur as a narrow haemorrhagic band round the papule. In such cases purpuric spots are frequently present. It may occur later as a black spot deeply situated in

the vesicle or pustule, as a general deepening of the colour of the contents of the lesion or as a dark red areola round it. In the vesicular and pustular stages this haemorrhage is most frequently found on the lower extremities and chiefly on the legs. It is seen often in the badly nourished and the vagrant class of patient, and in those who have not been confined to bed during the earlier stages of the attack. In similar circumstances it may occur in Varicella and in other eruptions consisting of local and particularly of vesicular lesions. More rarely it occurs in connection with lesions situated on the trunk or upper limbs.

That a purpuric rash may occur in the course of Smallpox is in itself a fact of some importance in diagnosis. But a like condition is met with in many other diseases of microbic and non-microbic origin. It is the frequency of its incidence in Smallpox and the severity of its manifestations in many cases, which enhance its importance as a feature of that disease. It is well therefore, in the investigation of such a condition to bear in mind, not only that Smallpox is a possible cause, but also that the probability of the presence of Smallpox increases in accordance with the intensity of the rash. It is not in errors in differentiation, but in the want of recognition of these



Petechial rash not due to Smallpox involving the flexor surface of the arm and the side of the neck chiefly, but avoiding the inner wall of axilla and side of the chest.

facts that mistakes have their origin. If the examination is made upon this basis, the failures to recognise the virulent forms of the disease will be few. But although the cases in which the diagnosis is

well In dealing with the subject of Haemorrhage in Smallpox, one has endeavoured to emphasise its more characteristic features, by an outline of actual cases observed at succeeding stages of the disease. On those features, in the majority of cases, the diagnosis is based. The sudden and severe onset, rapidly followed or accompanied by the typical general and brilliant erythema is not likely to be mistaken. At a later stage the deepening colour, the eruption of thickly set haemorrhages everywhere, the subconjunctival extravasation, the gradually increasing turgescence of the skin caused by the rise of the papular rash, the lividity, swelling and tenderness of the skin of the palms and soles, the condition of the tongue and mouth, are notable features.

The petechial rash affecting the groins and axillae in its denser forms is probably distinctive of Smallpox. Even when of minor intensity, if the grouped petechiae are limited to these situations, and the rest of the skin is free from eruption or shews patches of the reticulate erythema, in most cases the

diagnosis of Smallpox is justified. Among ⁶⁷98~~99~~ patients examined at the receiving stations, this groin rash was simulated in only one case.

But although the cases in which the condition is well developed, and the aspect of the patient is typical, are not easily mistaken, yet it is difficult to formulate distinctions by which in all cases the purpura of Smallpox may be recognised. The individual purpuric lesions are not distinctive in themselves, so that there remain certain cases in which, on account of the scantiness of the lesions, or the want of any characteristic distribution, difficulty is certain to arise. In such circumstances, one need only refer to the importance of a definite history of contact.

In young children, the most virulent type of the disease very rarely begins with the general erythema and not infrequently in the early stage of the attack the Skin haemorrhages are of the larger size, often circular and of a deep purple colour, but few in number and widely scattered. To obtain any history may be difficult. If the condition is not clearly attributable to some other cause the patient should at once be isolated on suspicion of Smallpox. In such patients, as a rule, opportunity is given for the development of the true rash.

In adult patients, a like difficulty arises much more rarely. But one may meet, at times, with the type of case in which haemorrhage appears only a short time before death. In the case described the sudden onset, the facies and general aspect of the patient, independent of a history of contact were very suggestive.

The value of purpuric conditions in the eruptive stage of the disease is secondary to that of the true rash. Not only are the individual haemorrhagic lesions wanting in distinctive characters, but also collectively they present no features which are comparable in constancy to those of the specific eruption. When the latter are deficient, the importance of the presence of haemorrhage is considerable, and in some difficult discrete cases, the recognition of the staining left by the fading petechial rash in its characteristic distribution is a valuable aid to diagnosis.

The importance of the early recognition of the purpuric manifestations of Smallpox is very great, for it is probable that the infectivity of the fulminant and rapidly fatal cases at least equals that of the more prolonged confluent or discrete attack. M.W. an adult female living in the N. district, was attacked by the virulent type of the disease. She shewed all the

signs of the intense toxæmia. It was not recognised. As far as one could learn she lived for four or five days, and during that time was visited and nursed by many of her neighbours and relatives. Subsequently no fewer than 20 patients were admitted to Hospital who owed their infection directly to this case. A similar history was not infrequent. But cases of this type are comparatively rare. In a total of 1763 patients admitted to Hospital in 1901, they numbered 67. The complete prostration of the patient and the rapidity of the fatal result also tend to limit their opportunities for spreading the contagion.

The majority of a population possesses some degree of immunity. They are susceptible to attack by the disease but not to death. Many of these patients suffer only very slightly from the toxæmia of the disease. When the prostration of the onset has passed off, or when the pre-eruptive period is completed, the illness is over and they are able to resume their usual life and so to come in contact with large numbers of unprotected individuals. The presence of "spots" may or may not cause remark.

As has been already pointed out, cases of this description are the most important cases in an epidemic. Their proportion is large. In 604 out of 1520

completed cases in 1901 such conditions were possible. In a considerable number they were present. For reasons already given it is unsafe to deal with such cases except from a purely objective standpoint. The diagnosis must be based on the characteristics of the rash and on these alone.

The characteristics of the rash are the individual and collective features of the lesions of which it is composed.

A. The Typical features of the Lesion.

The lesion takes origin in an intense and localised inflammation of the deeper layers of the epidermis. Hyperaemia of the papillae of the true skin is followed by swelling of the overlying cells of the rete mucosum and exudation of serum into the intercellular spaces. The cellular network thus formed becomes distended more and more as the exudation accumulates and as a result the lesion increases gradually and continuously both in size and prominence. But while growth is still going on retrogressive processes begin. Purulent change commences in the serous contents of the lesion, the remains of the cellular network are broken down and a surrounding inflammatory induration is produced. Healing takes place by the formation of a crust which,

after a time, is thrown off by the new epithelial growth which has taken place beneath it.

The morbid process thus outlined is represented clinically in the life history of the lesion. Appearing first as a macule, it passes gradually and regularly through the stages of papule, vesicle, pustule and crust. But, from the point of view of diagnosis, a systematic description of the varied changes in the clinical features of the lesion as its development progresses is of little advantage. It is preferable to attempt to indicate :-

1. the conditions which seem to be the important peculiarities in its morbid anatomy, and

2. how these conditions are represented, and can best be recognised in the clinical features of the lesion, at successive periods of its development.

1. The pathology of the lesion is essentially the life history of a vesicle. In this life history there are two stages, (1) the stage of formation, leading up to full vesicular development, and (2) the stage of retrogression, overlapping the former, beginning with the onset of purulent change in the contents of the vesicle and terminating with the disappearance of the crust. The peculiarities of the

process consist in its intensity, in its localised character, in its deep-seated origin and in the acuteness of its course.

The stage of Formation.

The early macule has no characteristic features. But the macular stage is very short, so short that usually in practice, one can recognise a distinctly papular element in the lesion which appears on inspection to be a simple macule. A subjective condition of some importance, especially at this very early stage, is the pain frequently associated with the lesion. This pain is described by the patient as a pricking sensation produced or increased by pressure on the area in which the lesion is situated. It is accentuated on parts where the lesion is bound down by thick and dense superficial strata, and therefore on the palms and soles it is sometimes useful as an indication of the site of a lesion which is obscured by dirt, or by the thickness of the horny layer of the epidermis.

The early papule is a smooth elevation, with a rounded summit and a glistening surface. An areola of varying and irregular breadth is often present. But the early lesion has no surrounding inflammatory induration. It is a small well defined thickening in the skin. It is hard. In its hardness or resistance,

the lesion is likened to a grain of small-shot embedded in the skin, and frequently attention is directed so closely to the making of this comparison, that the other and the more important condition is unduly neglected or altogether missed. That the smallpox lesion is hard, is true, but that it possesses a greater degree of hardness or is more "shotty" than some other lesions which are of similar appearance but of different pathology (a), is very difficult to ascertain. But such lesions are superficial in comparison with the lesion of Smallpox. Broadly stated, the latter is in the skin, the former, in the majority of cases, gives the sensation of being on it. In dealing with features, which, at best, can be only comparative distinctions and always must depend largely on the personal factor in observation, it is difficult to lay down tests which will appeal to any observer. But where the upper strata of the epidermis are relatively thick, the depth of the focus is the more easily recognised. On the palms and soles the early papule is scarcely raised above the surface. On passing the finger lightly over it, one perceives a very slight elevation with a gradual

- (a) Examples are (1) some lesions caused by the bites of insects when the acute stage has passed.
(2) many acne lesions.
(3) certain lesions of Varicella etc.

slope and a considerable area. With firm pressure the lesion assumes a smaller size and acquires a sharper definition.

There are certain conditions, depending on the intense and localised character of the process, which can be recognised by a close examination of the lesion, at a very early stage in its development. If one select for examination a lesion on the palm or sole, of recent origin and just palpable, it appears to the unaided eye as a simple macule, usually of irregular shape. But with the help of a lens, one can see, very frequently, near the centre of the spot, a tiny ring, of a tint distinctly paler than its surroundings, or the small area it encloses. As the lesion grows, the central area increases in size, the ring itself broadens considerably, acquires a more definite margin and becomes more opaque and white, so that, within twelve hours of its first appearance, the macule under the lens is resolved into three well marked zones. A narrow, perfectly circular and almost white belt separates a central erythematous area from an outer ring of erythema which varies in breadth. In a short time the condition becomes apparent to the unaided eye. This intermediate lighter belt (a) marks

(a) the appearance described may be seen in other lesions, e.g. Varicella on the palm or sole; but in none so well marked as in smallpox.



Sixth day of disease, shewing effect on the lesions of
the character of the epidermis in which they develop.

the periphery of the lesion and the outer erythema is the areola. As the central area increases in diameter it steadily darkens, becoming of a grey colour and translucent. This change is the result of the gradual accumulation of serous exudation beneath it.

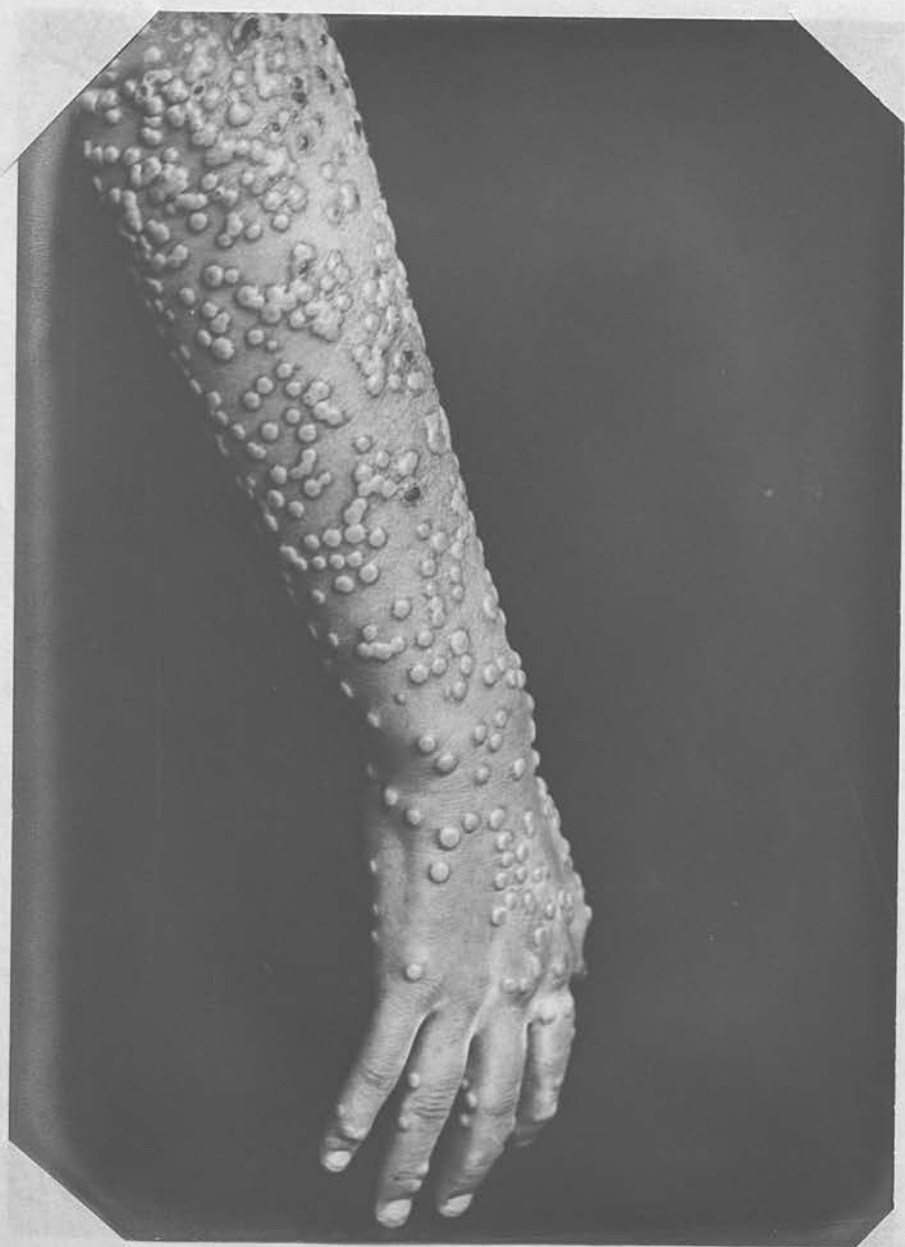
The main features of this vesicle depend on its situation in the skin. It is well defined. It develops beneath the dense superficial layers of the epidermis. Therefore its prominence varies with the thickness of these layers which are not involved in its formation. The vesicle situated for example on the palm of the hand is raised only very slightly above the surrounding skin. Such a vesicle therefore is not very refractile. It cannot be grasped, nor can it be ruptured by pressure. On the other hand, the vesicle situated where the upper strata are not so dense is more prominent and more refractile. If the skin is loose it can be grasped. But it conveys a feeling of solidity and it is unyielding as well as solid. It can seldom be ruptured by pressure and an attempt to rupture it causes considerable pain. The sensation of unyielding solidity imparted by a lesion which appears to be ^a translucent vesicle is a feature of considerable importance in differentiation.

It is of much greater value than the test by puncture of the lesion, a test into which of necessity the personal factor must enter largely. Nor is the umbilication of the vesicle a feature on which much reliance can be placed. It does not occur even in all typical lesions. It is transient and as a clinical fact is not peculiar to the lesion of Smallpox.

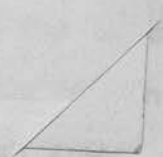
The Stage of retrogression.

While the lesion is yet small and on superficial examination still appears a clear vesicle, a lens will shew the beginning of pustulation. A slight milki-ness appears usually at its centre (a), and from the centre spreads to the periphery, so that the whole lesion becomes opalescent. In this opalescence the white peripheral ring becomes merged. This change goes on until the vesicle is completely transformed into a yellow pustule. During this stage the lesion increases greatly both in size and prominence. But clinically it is retrogressive. As development advances, the lesion gradually loses its characteristic features. As surrounding induration and oedema increase it becomes less definitely localised. As it

(a) The opalescence begins, in some lesions, at the periphery, appearing as a broadening of the peripheral ring.



Eighth day of disease . A few of the lesions on the back of the wrist shew the zones in the pustule which is in process of formation.



Pustulation advancing. Many lesions on the fingers show the zoned appearance described.

(a) "Lesions on fingers of the patient described."



Prosthetic hand and forearm with bumpy skin texture. The bumpy texture is a result of the prosthetic material used.

fills out with pus, the upper layers of the epidermis are more and more stretched and thinned and the internal cellular network is broken down. Therefore the sensation of unyielding solidity imparted by the vesicle is lost. It becomes more superficial and can be ruptured by very moderate pressure. Its tendency is to rupture, collapse and dry up to form a crust. Such crusts may be yellow or dark brown. They may be circular or elongated or of irregular outline. They may be flat or shew a gradual rise from the periphery towards a central point. In some, the margin is overlapped by the surrounding skin, so that they have been compared aptly to a jewel in its setting. (a) But none of these features is distinctive. The differentiation of the fully developed pustule or of the resulting crust does not rest on any individual peculiarities. It depends primarily on the recognition of the fact that the process which has produced them, has its origin in the deeper strata of the epidermis. Consequently it depends on their locality. Where the upper strata are thick and dense, the pustule does not rupture. Its contents are partially absorbed and the remainder with the pellicle forms the "seed" which is deeply embedded in

(a) "Lectures on diseases of the skin" No.xiii. Kaposi.

the skin. Such conditions are present to the most marked degree on the palms of the hands and on the soles of the feet, and therefore on these areas the most characteristic remains of the Smallpox rash are to be found.

Conditions which tend to produce variations in the features of the lesion.

It has been pointed out that the features of the lesion vary to some extent, with the structure of the epidermis in which it develops. But more important variations occur as the result (1) of conditions which disturb the nutrition of the skin, and (2) of the possession by the patient of a certain degree of protection against the disease.

1. The influence of disturbance of nutrition.

The lesions which present the most typical features throughout their development, are found in the discrete rash of the young, robust and unprotected individual. In such a case, the tissues react strongly to the onset of pustulation. An increase of pain and a deepening of the colour and broadening of the areola takes place, and oedema of the surrounding skin is produced. But, even in such a case, it can be seen that this reaction does



Fourth day of the disease. Severe discrete rash.



Ninth day in same patient. Showing marked reaction.
Modification is present but slight.

not occur to the same extent on every region. It is most pronounced on the face, hands and feet. It is present, but less marked, on the trunk, and associated with this relative deficiency in reaction, there is a tendency to variation in certain features of the lesion. On the trunk, the lesions tend to be less prominent, less regular in outline, and more varied in size, than those on the face and extremities.

The vigour of this reaction varies with the resisting power of the patient. With constitutional enfeeblement, it becomes deficient and in certain cases, it does not occur. In such cases the rash is said to develop badly. The period of eruption may be prolonged. The lesions, as they develop, become irregular in outline. The vesicles and pustules vary greatly in size. They are flat. They increase in area but not much in prominence. They tend to be flaccid and easily ruptured. Very many vesicles are never umbilicated and in many a puncture causes complete collapse.

Such variations in the features of the lesion are associated with general malnutrition. In the rash of the badly-nourished infant, or of the adult worn out by disease or by hard living, these atypical forms occur. They are closely associated with the more severe types of eruption. Frequently they are found

interspersed with haemorrhages on the trunk and limbs. They are the lesions which most frequently shew the haemorrhagic areola.

But, on the other hand, they are met with in certain of the mildest types of eruption and in such cases their recognition is of the highest importance. Not infrequently, the rash of old and infirm or helpless patients is most discrete. Their skin shares in their general condition of senility or malnutrition and in many patients of this class anomalous forms of lesion are the rule.

The influence of certain skin diseases, such as Eczema or Psoriasis, is more evident in partial disturbances of the distribution of the lesions, than in any marked variation in their clinical features. But generalised conditions such as Ichthyosis or even an abnormal dryness of the skin, seem, in certain cases, to interfere with the development of the rash and to produce variations, similar in tendency but less profound than those described as the result of a constitutional debility.

3. The influence of the presence of a degree of protection against the disease.

The influence of a partial immunity to the disease, in the patient attacked by small-pox, causes



Tenth day of disease. Rash modified by Vaccination
showing decrease in size and well-marked variation
in size of lesion, with moderate tissue reaction.

variation in the features of the lesion, by diminishing the intensity of the morbid process which produces the rash and which constitutes its development. This modification of the process takes effect in two directions. There is a decrease, on the one hand, in the number of its foci, and on the other, in its intensity in each focus. To the latter, the changes in the features of the lesion are due.

These changes vary with the degree of the immunity. They are associated with a general decrease in the size of the lesion and with an accentuation of the variation in size which is a feature even of the unmodified rash. They are associated also, with a shortening of the life-history of the lesion. Such shortening may occur to any degree. The lesion may pass through the complete sequence of its development, but with greater rapidity, or a true abortion of the process may occur. Crusting may take place very early in the stage of vesicle formation, or the area of vesiculation and pustulation may be restricted and appear not to involve the whole lesion.

It is impossible to describe all the variations which may occur in the features of the lesion, under the influence of conditions which seem to tend ultimately to effect the complete disappearance of the rash.

The typical features of the lesion are at best only comparative distinctions. The general decrease and the marked variation in the size of the lesions, render the recognition of these features more difficult. The early papule appears more acuminate and less deeply set in the skin. The lesions may never become fully vesicular. Frequently, the vesicle, pustule and crust appear as if set on the top of the papule. The small size of the lesion causes difficulty in the appreciation of the solidity of the vesicle, which is more superficial, more easily grasped and frequently more easily ruptured than the vesicle of the unmodified rash. There is a decrease in reaction with the decrease in the area of pustulation. Frequently the pustule is not only small, but also irregular in shape and the resulting crust tends to be thinner, more irregular and more superficial than the crust of the unmodified rash.

On the other hand, such variation in the features of the lesion is always less in degree on the hands and feet, than on the face, trunk and upper parts of the extremities. Under the influence of immunity, variation in the individual lesion usually increases with decrease in the density of the rash. But in the majority of eruptions, even the most discrete, although

the lesions on all other regions are changed quite beyond recognition, those on the palms and soles retain certain of their typical features. In addition, in the case in which opportunity is given for a short observation of the patient, the increased rapidity of the process which, even in its unmodified form, runs a course both acute and continuous, is a valuable aid to diagnosis.

B. The Typical Distribution of the lesions.

In the manner in which the lesions affect different areas of skin, a contrast between the head and extremities on the one hand and the trunk on the other is at once apparent. If one examine the confluent rash as it occurs, for example, in the unvaccinated child, it is evident that the eruption affects the head and extremities much more severely than it affects the trunk. Cases of this description, in which the inequality in the distribution of the rash is so apparent, are not usually mistaken. Such a rash certainly shews the typical Smallpox distribution. But it shews the distribution, in a manner so exaggerated, if one may say so, that certain of the features, on which its claims to be described as typical are based, are apt to be lost sight of, or at least not fully appreciated. That this is so is evident from



Tenth day of disease, shewing the typical distribution.

the fact, that mistakes in diagnosis occur, not only in cases of Smallpox in which, while the distribution is perfectly typical the total number of lesions is small, but also in cases not Smallpox in which, while the typical distribution is entirely wanting, the lesions are thickly set both on head and extremities.

The typical distribution of the rash of Smallpox does not mean simply that the head and extremities are more affected than the trunk. It must be understood that it is to the density of the rash that reference is made. If, for example, one compare the rash on the face and scalp with that on the trunk, it will be evident in many cases, that the number of lesions on the trunk much exceeds the number on the face and scalp. But, if one take into account the relative size of the areas affected, it is evident at once, that the density of the rash on the face and scalp very much exceeds its density on the trunk. As one may express it, the average distance between two lesions on the trunk greatly exceeds a similar measurement on the face. In the same way the density of the rash on each of the extremities exceeds its density on the trunk. But in the distribution of the rash as it affects the extremities, there is another feature which must be taken into account. The genuine rash of Smallpox,

however discrete, in which lesions are not found on the hands and feet is exceedingly rare, and a rash which is of considerable density on the upper parts of the extremities, which decreases in density along the forearms and legs and avoids or only very lightly affects the hands and feet is, almost without exception, not the rash of Smallpox. In its distribution, then, on the extremities, the rash of Smallpox has a well-marked tendency to affect the distal rather than the proximal parts, and not to decrease but rather to increase in density with distance from the trunk.

Such are the two main features of the typical Smallpox distribution, the one, a general feature applicable to the whole rash, the other, a special feature applicable to the rash as it affects the extremities.

In the examination of a suspected eruption both features must be considered. The one is the complement of the other. The importance of making a complete survey of the skin and of obtaining, if possible, a "bird's eye view" of the greater part of the surface, is evident. In the confluent or severe discrete rash, this general survey is in most cases sufficient for recognition of the typical distribution. But, in mild discrete eruptions, the comparison of one region



Ninth day of disease. The typical distribution.

that of smallpox.

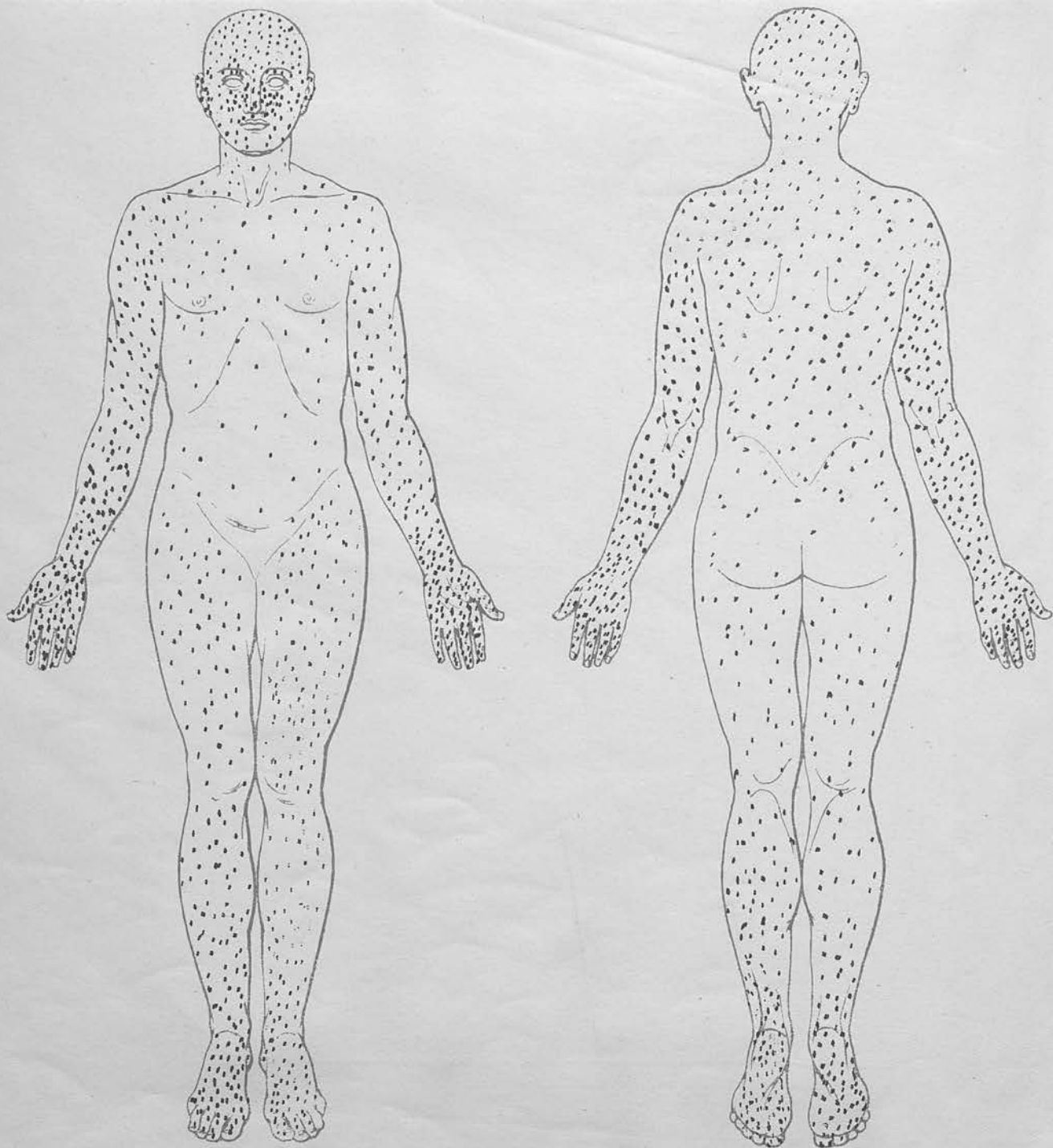


Varicella, shewing contrast in its distribution to
that of Smallpox.



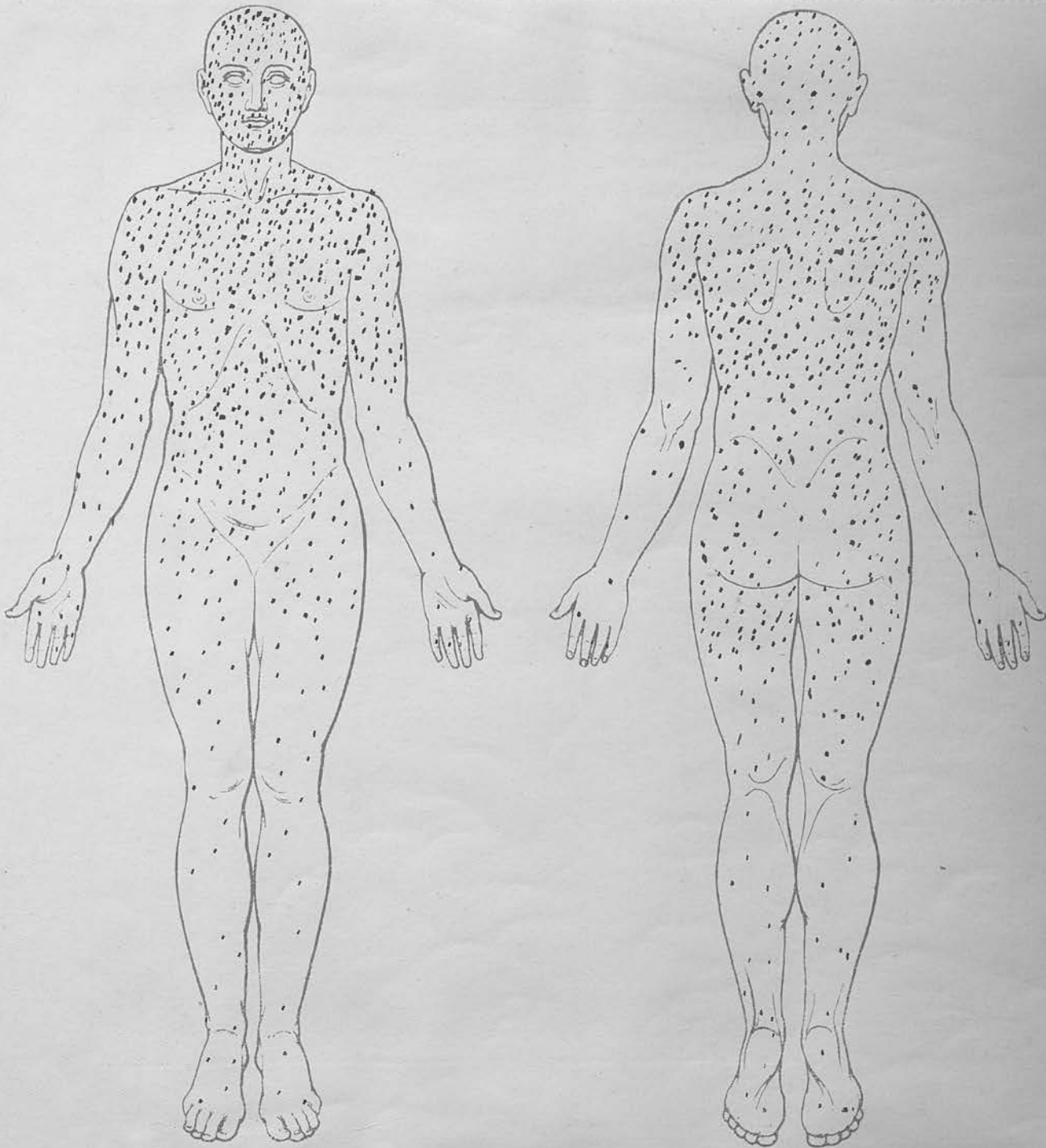
Varicella, shewing a distribution which is negative
to Smallpox.

The typical Distribution.



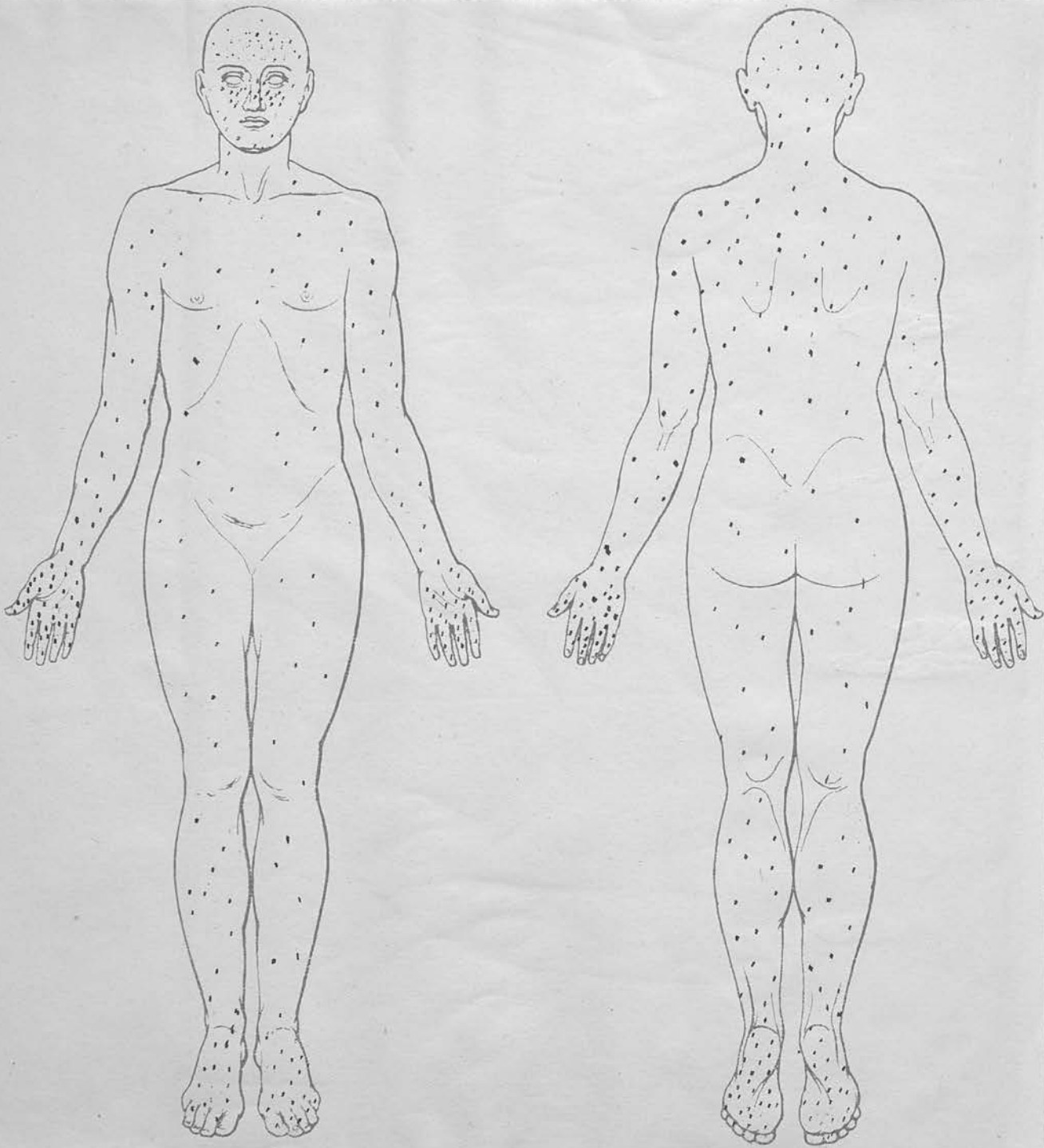
The typical severe eruption.

The Typical Distribution.



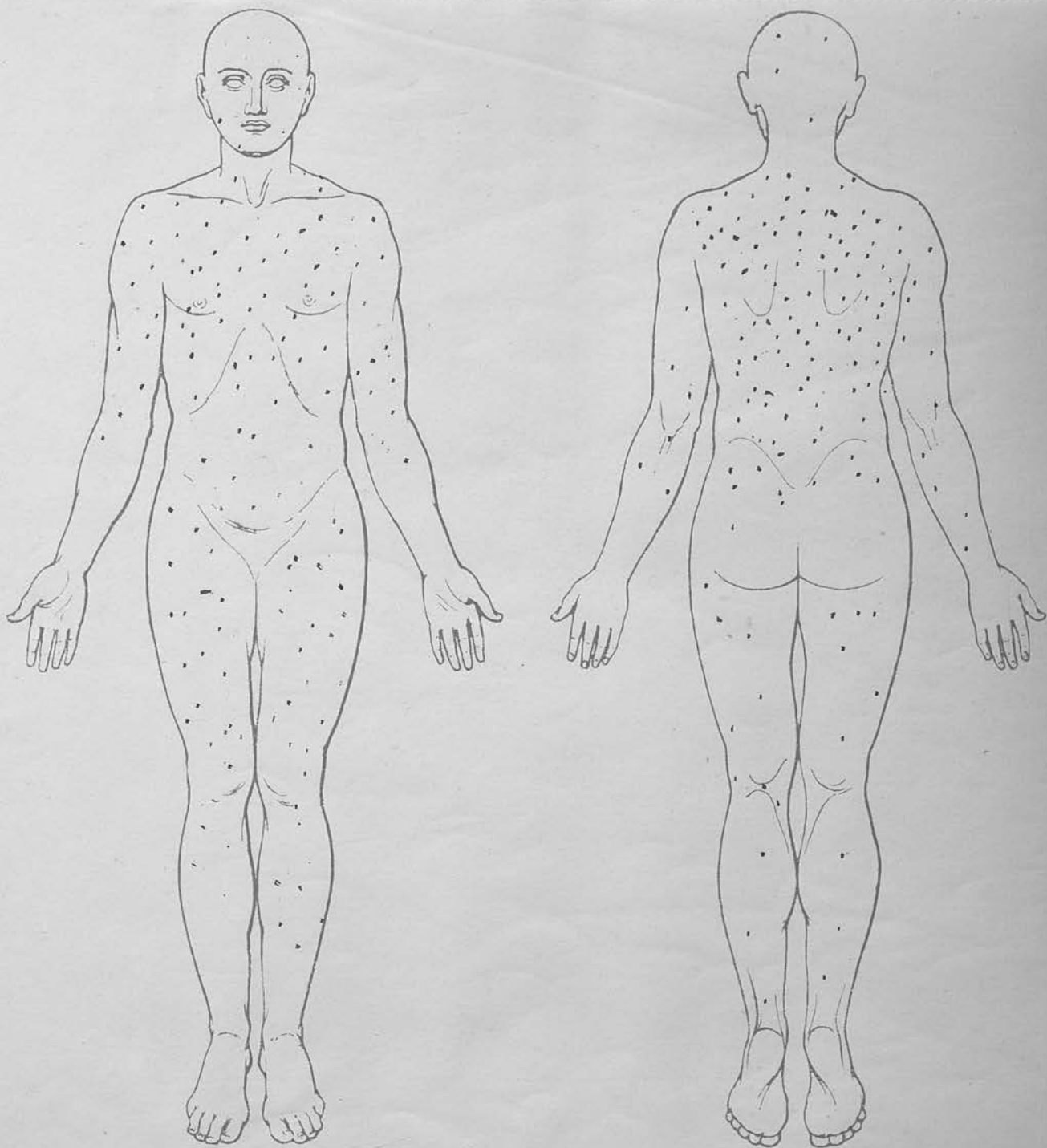
Severe eruption which, almost certainly, is not
Smallpox.

The Typical Distribution.



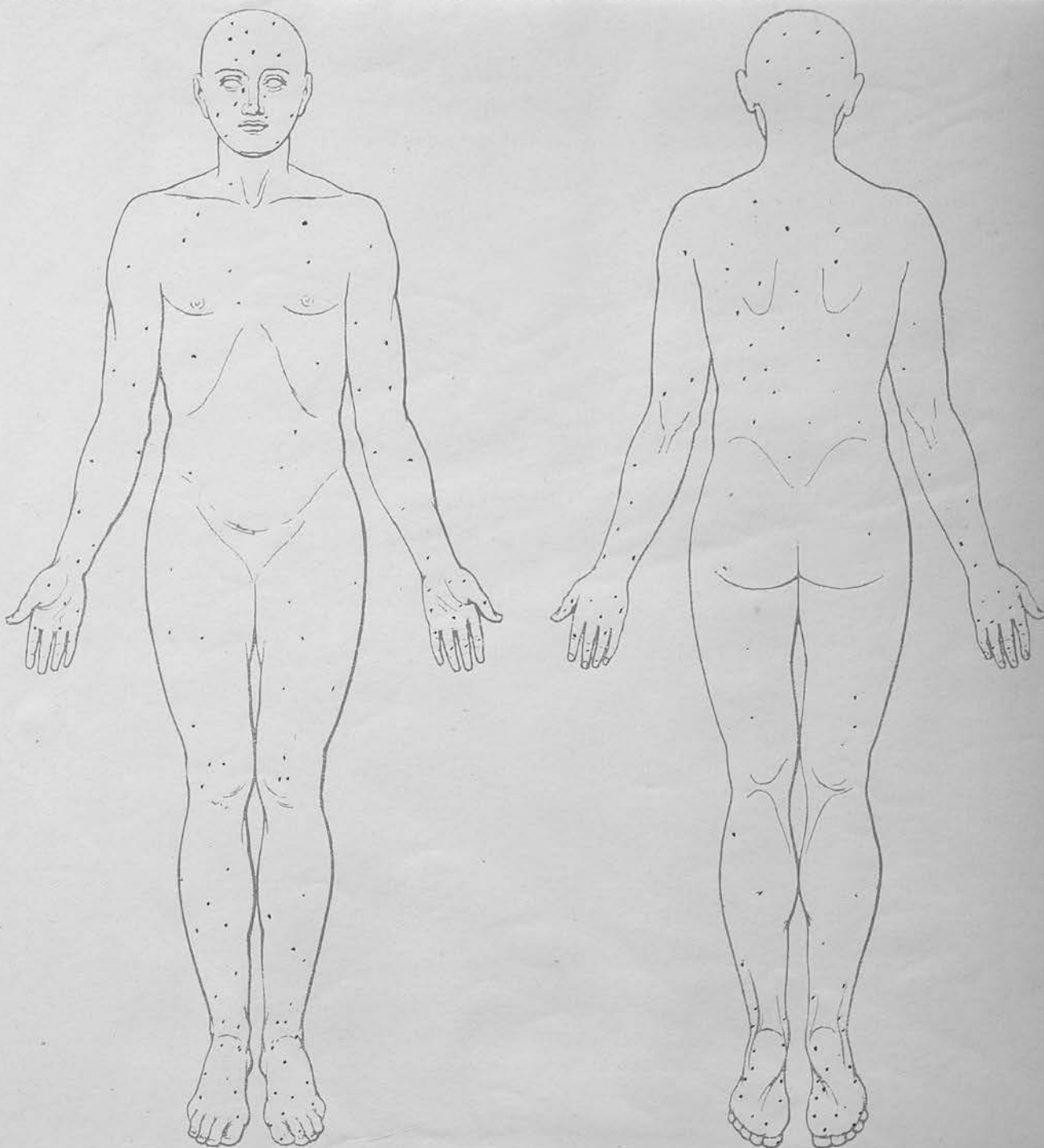
A less severe typical eruption.

The Typical Distribution.



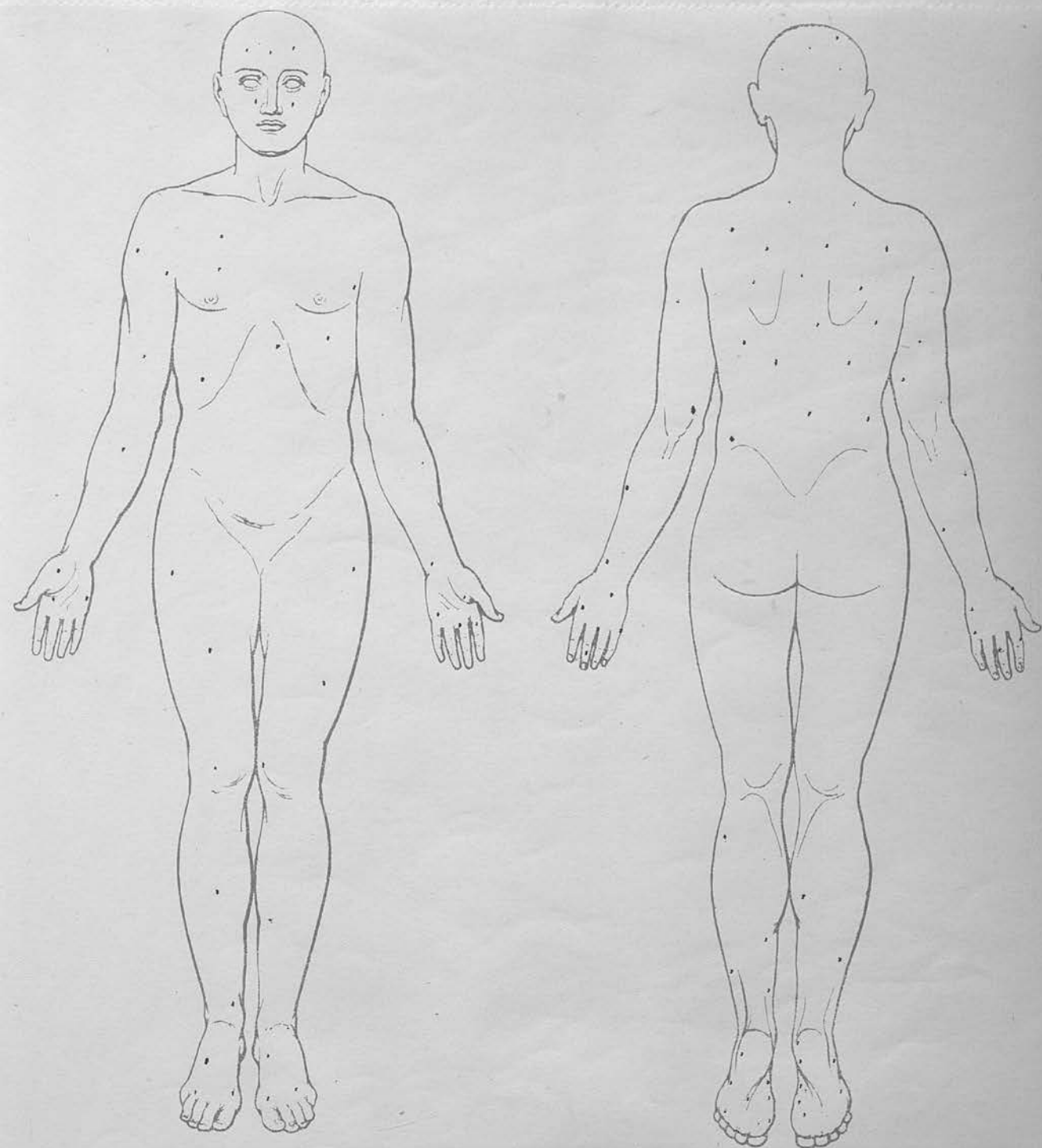
Moderately severe eruption which, almost certainly is
not Smallpox.

The Typical Distribution.



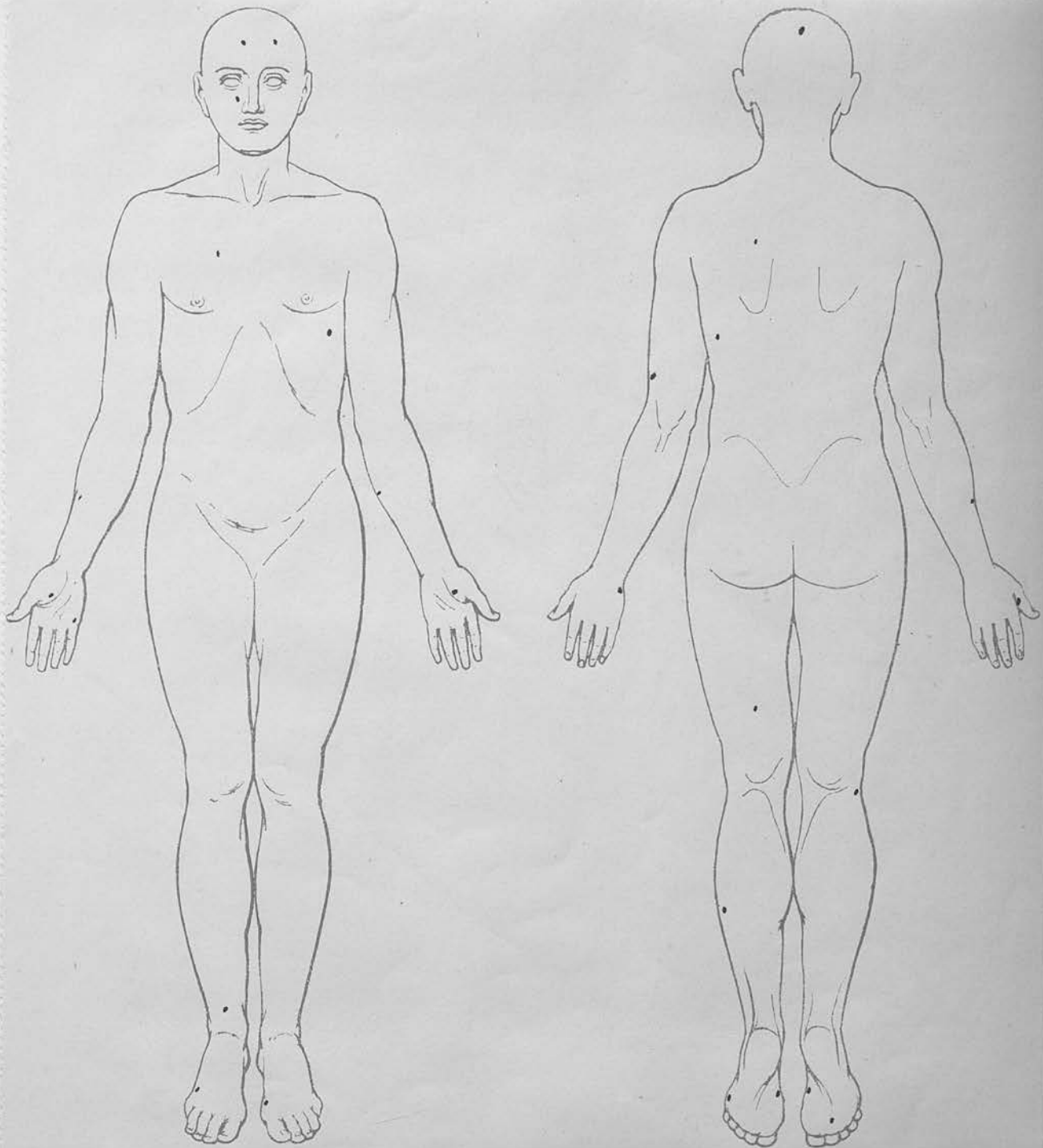
A typical discrete rash.

The Typical Distribution.



A typical very discrete rash.

The Typical Distribution.



A typical most discrete rash.

with another can only be made after a careful and detailed examination of the different areas. In making this examination one must not attempt to compare a selected area of one region with a selected area of another. For example, it is fallacious to compare a small area of the trunk with the face or with some part of the arm or thigh. The whole region must be taken into account in the comparison. And again, one must not expect that, on the extremities, the density of the rash in every case increases, in a gradual and uniform manner, from the shoulder to the hand or from the groin to the foot. If these points are kept in view, the recognition of the typical distribution, even in the mild discrete rash, in the great majority of cases, is attended with little difficulty.

A - typical Distribution.

But, although, in the great majority of all cases of the disease, both features are present, there are certain cases of undoubted Smallpox, in which the distribution of the rash does not completely conform to type.

It is evident that it may not be possible to recognise the typical distribution, in cases which are ^{not} seen during the actual period of eruption. But this

is scarcely a practical difficulty. The actual period of eruption is short. All regions of the skin are invaded by the rash in rapid succession and in many cases, the invasion of every region is practically simultaneous. The cases in which lesions cannot be found on the hands, if not on the feet, in a very few hours from the beginning of the period of eruption are very rare.

Again, as the patient is approaching the end of his convalescence, when the last traces of the rash have disappeared from face and trunk and the remains of the eruption are to be found only on the hands and feet, it is evident, that the test of the typical distribution, must be supplemented by a recollection of the essential features of the pathology of the lesion.

In the majority of the cases in which defects occur, they can be ascribed to local and accidental conditions which increase or decrease the incidence of the rash, on the parts of the skin which they affect.

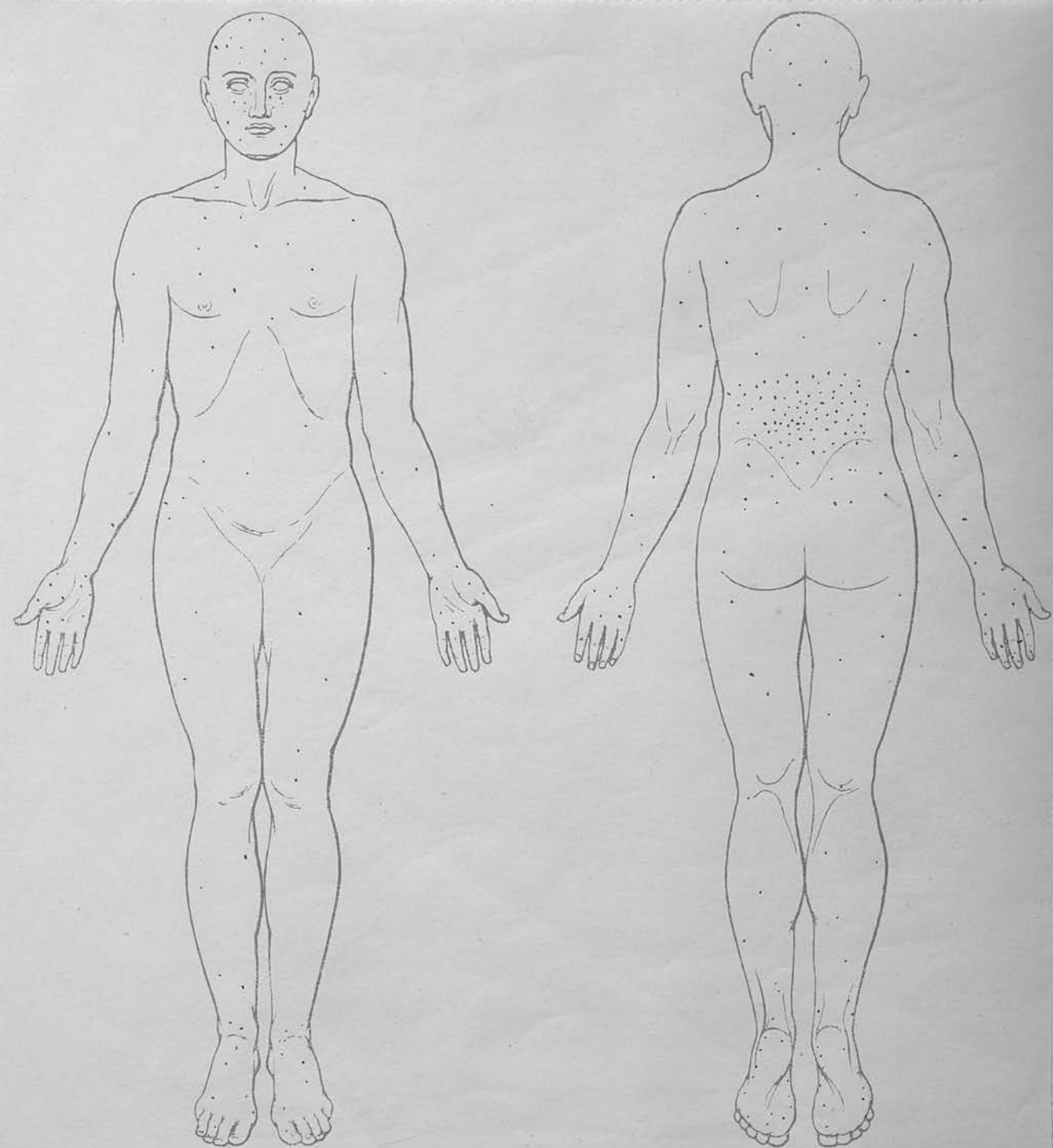
An increase of the incidence of the rash on the trunk or upper arms or a decrease of its incidence on the hands and forearms or on the feet and legs, will bring about divergence from the typical distribution.

a. Conditions which act in the former way, are the more common in the class which Smallpox attacks.

The following illustrative cases are taken from many which occurred during the epidemic. A patient suffers from severe pain in the back during the pre-eruptive stage. A mustard plaster is applied and on the site of its application a very dense and almost confluent rash develops, while the rash on the face and on the rest of the body is quite discrete. The child who is neglected and whose buttocks, thighs and abdomen are irritated by a diaper constantly saturated with urine, frequently shows, on these parts, a rash much more dense than on the rest of the body. The nursing mother who suffers from cracked nipples often develops a dense rash on the breasts, and the condition is much accentuated if a crack has been the site of inoculation of the disease by the suckling. Round a wound, on a recent scar, along the scratches and round the sores resulting from the presence of pediculi, scabies or some old-standing skin disease, the incidence of the eruption is increased.

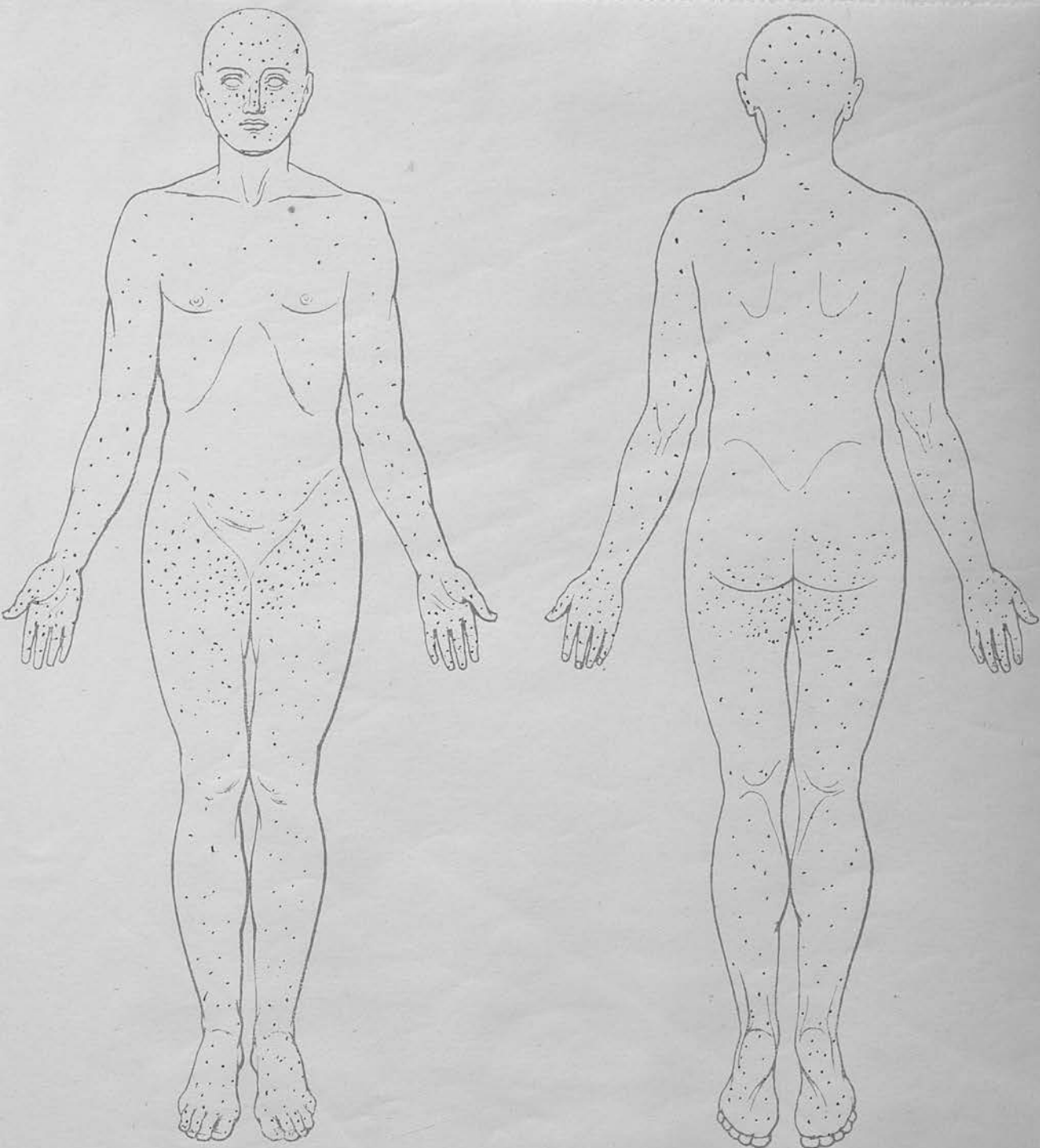
Such conditions frequently affect large areas of the skin of the trunk and upper parts of the limbs. But all may be described as irritative in their action. The increased incidence which results, is local, and almost invariably so obviously the result of such action, that its influence is easily discounted in the examination of the comparative distribution.

The effects of irritation, environment, etc.



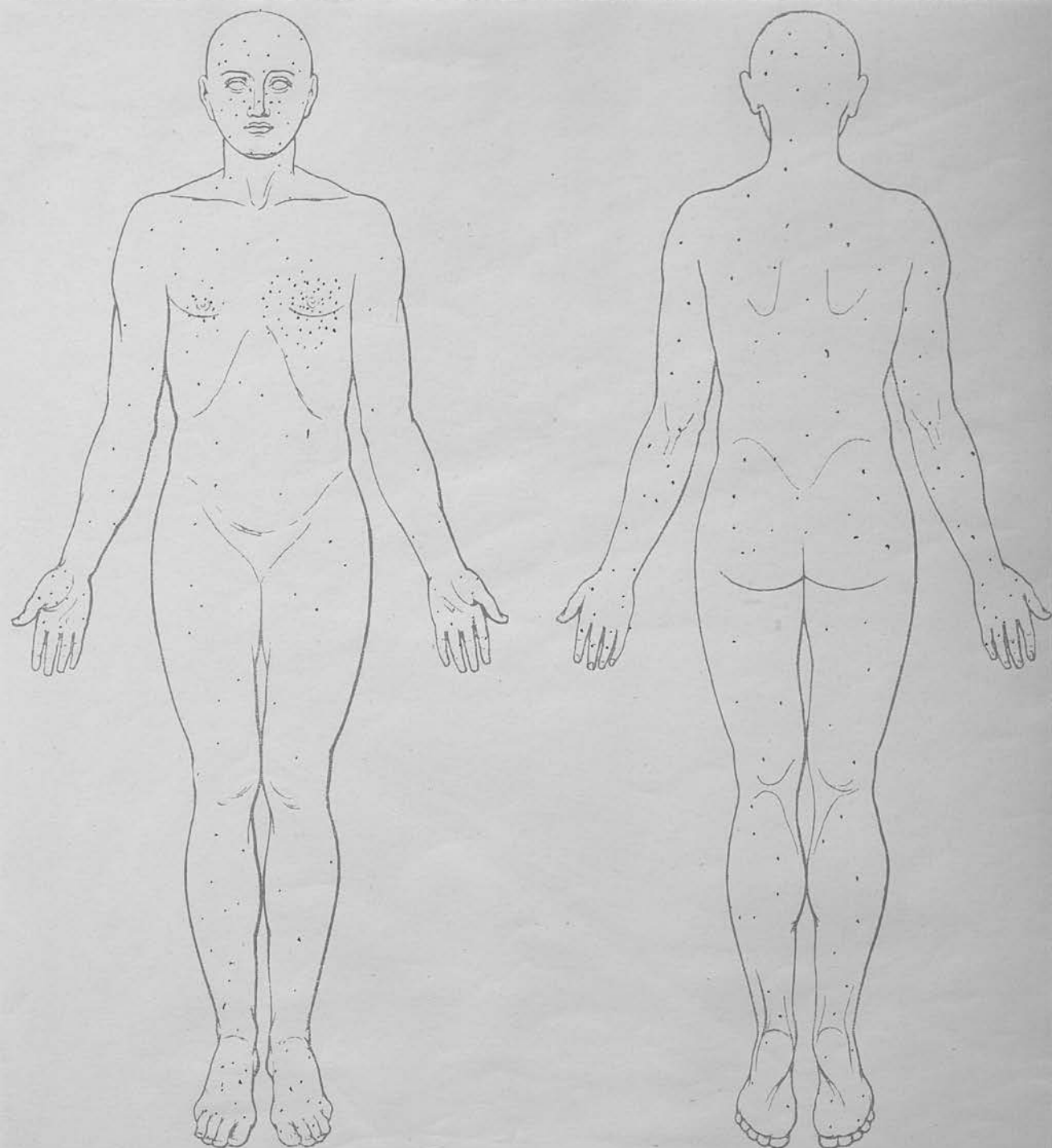
Effect of external applications.

The effects of irritation, environment, etc.



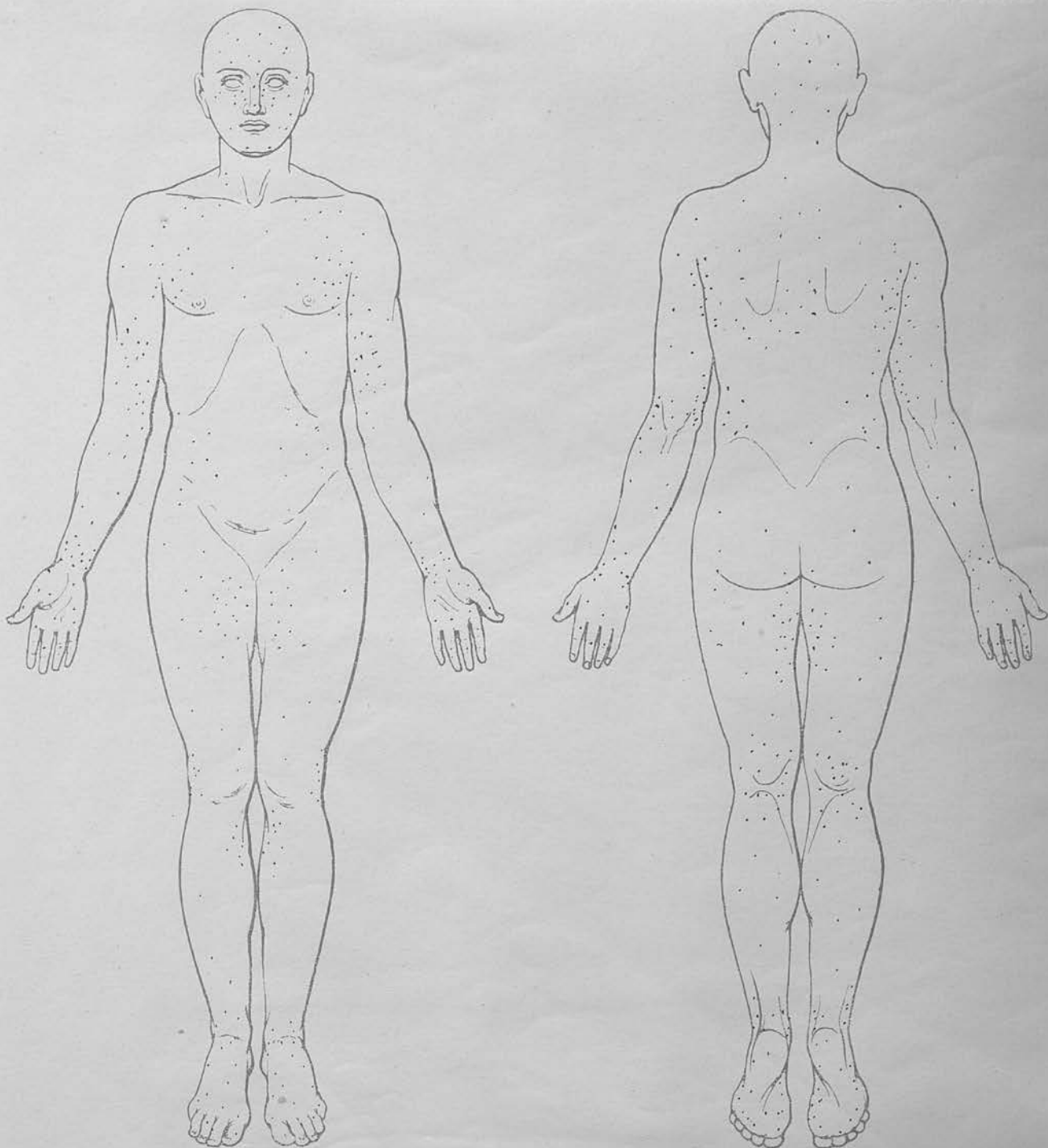
The neglect of cleanliness.

The effects of irritation, environment, etc.



The rash of the nursing mother.

The effects of irritation, environment, etc.



The effect of old-standing Skin disease (Scabies).

b. Conditions which influence the distribution by tending to decrease the incidence of the rash on the extremities are less frequently present, but their result is not less important.

In contrast to the former which are irritative, these conditions are protective in their action. They are associated mainly, with the occupation and environment of the individual. It is extremely rare for any disturbance to take place in the comparative distribution in regard to the face. But, in some genuine eruptions, the distribution may be defective in its first feature in regard to the extremities. That is to say, the density of the rash on the arms or on the legs, may not be obviously greater than the density of the rash on the trunk. This partial defect in distribution is not uncommon in patients who have acquired Smallpox in Hospital, after long confinement to bed.

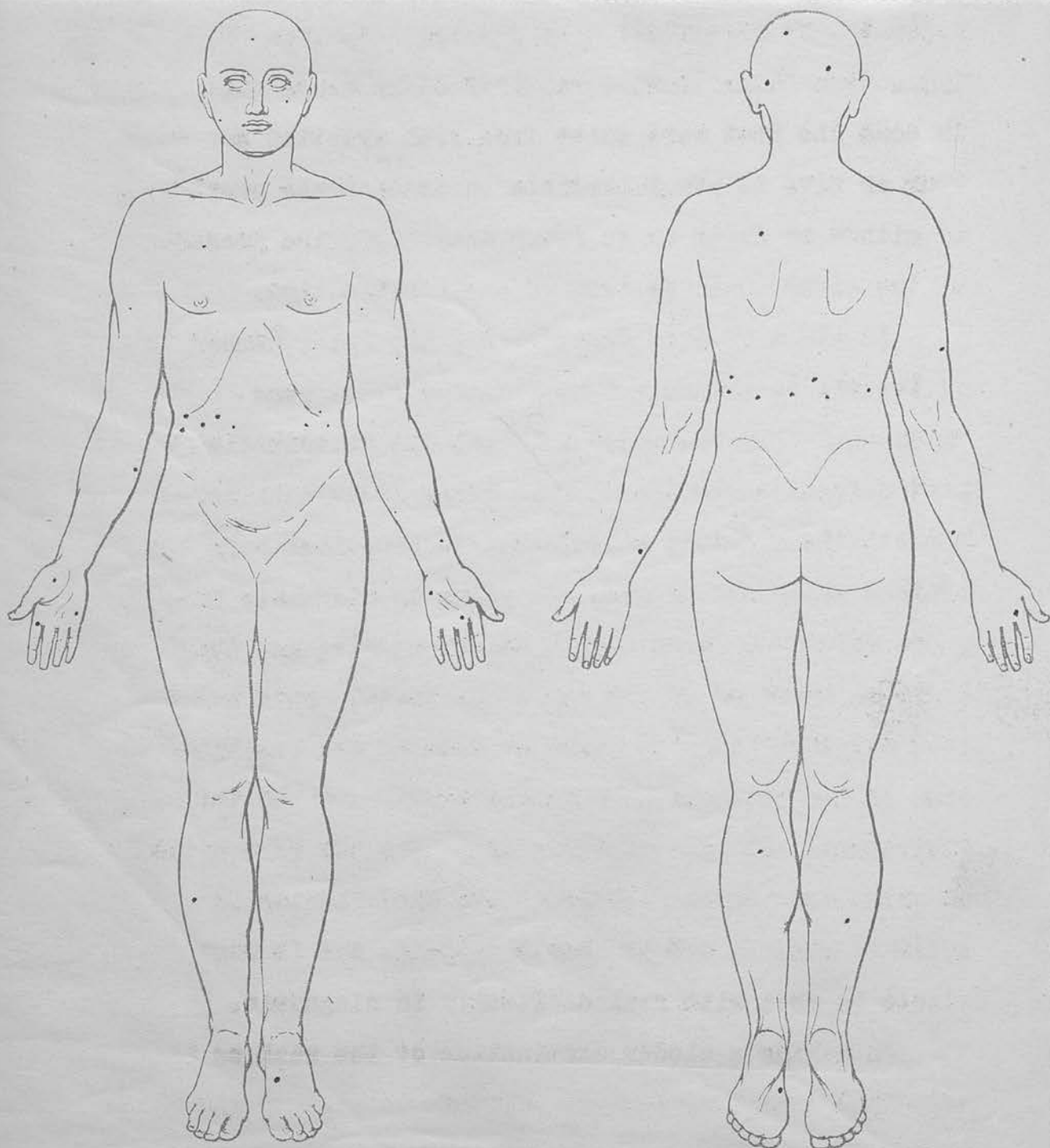
But the case in which this partial defect is found in both upper and lower limbs very rarely occurs, and the case in which the density of the rash is obviously less on the limbs than on the trunk is still more exceptional.

Of all departures from type, the most common is a partial defect in the special feature of the

distribution as it affects the limbs. In some cases the density of the rash does not increase and in a very few cases it certainly decreases with distance from the trunk. It is not usual, for example, for the hands of the clerk, to shew as large a crop of lesions, as the hands of the man who is constantly engaged in hard manual labour. The feet of the patient who is attentive to personal cleanliness tend to shew a less severe rash than those of the tramp. But it is very exceptional, in genuine smallpox, for both arm and leg to shew this partial defect in distribution. It affects the upper more commonly than the lower extremities, and the true Smallpox rash which entirely avoids both hands and feet is the greatest rarity.

In a remarkable series of cases admitted from one of the large Poor-law Infirmeries, there were twenty women all over fifty years of age. Many of these were bedridden. All were practically helpless. In many, the influence both of environment and of irritation were illustrated. Very few had a severe rash. In several, the total number of lesions did not exceed fifty and in four or five it was less than twenty. The majority of the lesions in many were on the trunk and were arranged along the line of pressure

The effects of irritation, environment, etc.



A rash in a helpless patient.

exerted by the waistband of the dress. But in the majority the distribution of the rash was true to type. The first feature was present in every case, but in some the feet were quite free from eruption and in four or five it was impossible to demonstrate completely either on upper or on lower extremity, the presence of the second main feature of the distribution.

In cases of this description, the total number of lesions is always very small, and it happens invariably that the rash, in which the distribution is most defective, is the rash in which individual lesions exhibit the greatest variation. In practical work the lesions which are of greatest value in diagnosis are those which are found on the hands and feet and especially those situated on the palms and soles. This holds good not only from the point of view of the distribution of the rash but also in the examination of the individual ^{lesion.} It follows therefore, that the rare cases, in which the second feature of the distribution is entirely absent, are the cases in which one is most liable to meet with real difficulty in diagnosis.

On making a closer examination of the rash as it affects the various regions, certain details in its incidence are evident. Although of minor importance, these details are sometimes of value in diagnosis as



Tenth day of disease, shewing tendency to central grouping of the lesions on the face and well marked reaction.

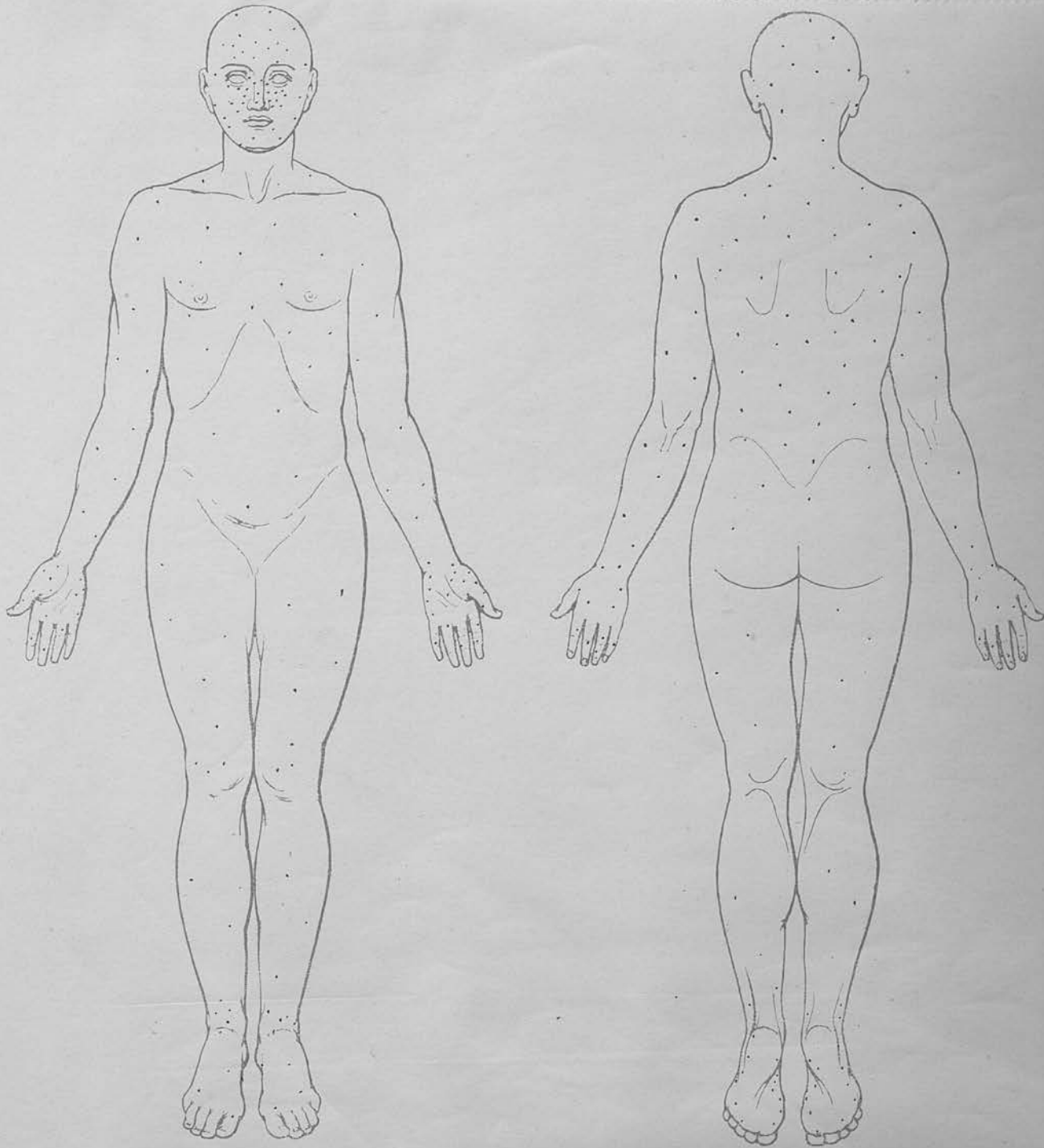
supplementary to the two main features of the distribution.

The Face is always affected by the rash and always to a greater degree than the scalp. The density of the rash on the face is almost invariably greater than its density on any other region. In many cases the lesions on the face shew a tendency towards a certain grouping. A considerable proportion of the rash is usually situated on the forehead, where the lesions are irregularly scattered over the central part and on the skin between the eyebrows. If these areas are free and the great majority of the lesions on the forehead are grouped along the margin of the hairy scalp, there is a strong presumption that the rash is not that of Smallpox. The area, roughly triangular in outline, bounded by the ridge of the nose and the lower margin of the orbit and a line from the angle of the mouth to the outer canthus, is affected, usually to a greater degree, than the parts of the face outside and below it. If this area is free, while the lesions are grouped on the skin over the lower jaw, the chin and the other parts of the cheeks, the rash is more probably due to some other disease than to Smallpox. On the face generally, the tendency is for the grouping of the lesions to be central rather than marginal.



Two photographs of the same patient, shewing the typical distribution on the trunk. The density is greatest on the back and greater on the chest than on the abdomen.

The Typical Distribution.



The less important details of the distribution.

On the arm, the rash is irregularly scattered, but on the hand, the lesions are usually more numerous on the palm than on the back. On the palms, the thenar and hypothenar eminences are favourite sites.

In a similar manner, on the foot, the lesions are usually more thickly set on the sole than on the dorsum. The inner margin following the arch of the instep is a favourite site.

On the leg, it is not infrequent for the majority of the lesions on the anterior surface to be grouped on the skin just above the ankle joint.

Almost invariably the rash is more dense on the back than on the front of the trunk and the majority of the lesions on the front are situated on the chest. Not infrequently, the skin of the abdomen is almost entirely devoid of eruption. The rash has a well marked tendency to avoid the parts affected by the petechial primary rash, so that frequently, on the groins, flanks and outer and inner walls of the axillae, very few lesions are seen.

C. The typical correlation of lesions and groups of lesions in their distribution and development.

In the unmodified (a) attack of Smallpox the

- (a) The rash, the lesions of which are affected neither by a partial immunity nor by accidental conditions.

period of eruption (b) usually begins at the end of the second day. Lesions continue to appear throughout the third and in some cases on the fourth day of the disease. It has been pointed out (c), that in such a case, the first lesions to appear are a few on the face and that invasion of the trunk, arms and hands, legs and feet, follows the appearance of the rash on the face. But, in practice, an opportunity for observing the actual beginnings of the eruption is comparatively rare and the fact that lesions first appear on the face has no differential value. Nor is there, in any case, any advantage to be gained, by an attempt to discover some sequence in the invasion of the various regions by a rash of which the eruption is well advanced. On the other hand, that, early in the eruptive period, lesions have appeared on the extremities and chiefly affect the parts most distant from the trunk is an observation of considerable importance.

The development of the typical lesion is a gradual, continuous and regular process. Therefore, those lesions which were the first to appear, will tend, throughout their development to maintain their

(b) The initial lesions of inoculated Smallpox are not referred to here.

(c) Gurschmann on Smallpox in Ziemssen's Cyclopaedia of Medicine Vol.ii.

priority. The clinical features of the typical lesion are influenced by the nature of the epidermis in which it develops, so that those lesions which are situated on the same region and, more especially, those which are in proximity to each other, will tend to resemble each other closely at corresponding stages of their life history. If they were synchronous in their eruption, they will be synchronous in the successive stages of their development. It seems to follow, that the rash which shews a certain sequence in its invasion of regions, will shew a similar sequence in its subsequent development and that the lesions which are situated on the same region, will arrive at the successive stages of their life history approximately at the same time.

There is no doubt that in certain eruptions, these features can be recognised, especially during the later stages of the development. But their value in practice is limited.

The whole period of eruption does not extend usually beyond thirty-six hours, and in every case within a very short time after the appearance of the first lesions, others can be found on almost every region of the skin. Certainly, in the great majority of cases, the invasion of the hands and arms follows



Tenth day of disease, shewing priority in development
of rash on face.

very rapidly on the invasion of the face. In a severe attack the face shews, at the outset of the eruptive period, a much larger number of lesions than are seen on other areas of similar size. But it does not follow that this superiority depends entirely on a priority of invasion. Probably, it is associated as closely with the fact, that the density of the rash on the face, when eruption is completed, is greater than its density on any similar area. At its highest value, the priority of invasion of one region over another, can refer only to the majority of the lesions which affect these regions, and, in practice, it is difficult, in many unmodified cases, during the first days of the development, to detect a distinct priority in any region.

On the other hand, as the rash progresses, the lesions on the face and scalp acquire a definite priority, while those situated on the hands and feet and particularly those on the palms and soles, seem to lag behind in their development. (a) In the end, the desiccated remains of lesions are to be found on the palms of the hands and on the soles of the feet,

In diagnosis, is limited, in any case, to certain

(a) That is to say, this priority is a matter of development rather than of invasion, and probably, depends more on the character of the skin in various regions, in respect of its nutrition and density, than on sequence of invasion by the rash.

at a time, it may be weeks, after all traces of the rash have disappeared from the rest of the skin.

The importance of the recognition of this fact in the examination of suspects, has been already pointed out.

The features of importance in the typical relationship of lesions and groups of lesions may be thus summarised:-

1. The early appearance of lesions, not only on the face, but also on the extremities.
2. The early appearance of lesions, in the great majority of cases, on the hands, and in many cases also on the feet.
3. The essential similarity in type and in development of all the lesions, a similarity most easily recognised in the earlier stages.
4. The definite priority of the lesions on the face in the later stages.
5. The persistence of the remains of the rash on the hands and feet, after it has disappeared completely from the rest of the body.

It is evident that the value of these features in diagnosis, is limited, in any case, to certain periods of the development. But the value of some is restricted, in many cases, by other conditions.

Local irritation, by increasing the density of the lesions on the areas affected, causes apparent, if not actual disturbance in the sequence of invasion. A defective state of nutrition, by increasing the variation in the size and contour of the lesions, tends rapidly to obscure the evidence of their similarity in type. Such conditions not uncommonly affect the class from which the majority of Smallpox patients is derived.

The presence in the patient of a partial immunity to the disease, less seriously disturbs these features. In decreasing the density of the lesions, it tends to shorten the period of eruption and to render the whole rash more simultaneous both in eruption and in development. In curtailing the period of development, in such a rash, it tends to accentuate the similarity of its lesions in their later stages.

It is clear, therefore, that it is unsafe to regard the absence of some definite sequence in the invasion of regions or the absence of a marked similarity in the type of the lesions, even of those situated in close proximity to each other, as reliable negative evidence in diagnosis. But, in the great majority of every class of case, the lesions which affect the face, gradually assume a definite lead in development, while

those which affect the palms and soles, are, in many cases, among the first to appear and in every case the last to remain.

D. The comparative differential value of the characteristics of the rash of Smallpox.

Of the characteristics of the rash, the most reliable in differentiation is the distribution of its lesions.

1. It is the feature which is most constantly found in the genuine eruption.

The distribution of the rash is associated with the position of the lesions and is independent of the changes which constitute the development. On these changes the other features of the rash are based. It follows that in the cases in which it is present, the typical distribution must be the most persistent feature of the rash. But it is also the feature which is least subject to disturbance. Being independent of the morbid process which constitutes the development, it is independent of the conditions which influence that process. It is unaffected by the presence in the patient, either of a partial immunity to the disease or of a general condition of malnutrition. These are the conditions which most frequently are responsible for variation in the features of the rash.

It follows, therefore, that the distribution is the feature which is not only the most persistent but also the most constant in any series of genuine Smallpox eruptions.

2. It is not found in those eruptions which are

most liable to be mistaken for Smallpox.

An analysis of the cases in which the diagnosis was revised, occurring in an epidemic in a population such as that of London, should afford a fair estimate of the diseases most liable to be mistaken for Smallpox.

(a) From Jan. 1st to Dec. 31st 1902, 7842 patients were admitted to the Receiving Station. In 607 of these the diagnosis was corrected. If one select the cases in which there was evidence that the diagnosis had been based on the presence of an eruption more or less resembling the rash of Smallpox, the following table may be constructed :-

	<u>Corrected diagnosis.</u>	<u>No. of Cases</u>
1.	Varicella	203
2.	Measles	48
3.	Acne	42
4.	Eczema	31
5.	Lichen	26
6.	Herpes Iris	2
7.	Impetigo	4
8.	Pemphigus	2
9.	Scabies	11
10.	Drug rashes (Eromide etc.)	3
11.	Syphilis	30
12.	Scarlet Fever	4

(a) Statistics of the Metropolitan Asylums Board

Smallpox Receiving Station. Report for 1902.

13. Vaccination rashes

3.

14. Dermatitis due to Insect bites

unclassified papular erythemata etc.

Varicella

The cases of this disease numbered 203 out of a total of 607. (a) Fourteen were patients over 25 years of age. One was 36, another was 49, and another was 54. In many, the lesions were much disturbed by secondary infection, resulting in the production of well marked pustulation, with surrounding induration and an irregular and thick crust. In many, the lesions on the face, hands and arms were round and hard. That these lesions were more superficial than those of Smallpox was difficult to ascertain. In one child the site of the lesion was the centre of a small patch of gangrenous skin. But in none was the typical Smallpox distribution present. In many the lesions were as densely set on the face as on the trunk and in some the comparative density of the rash on the face was compatible

(a) the following statements are based on the cases admitted during the first nine months of the year. The total number of negative cases admitted during the last three months was 20.

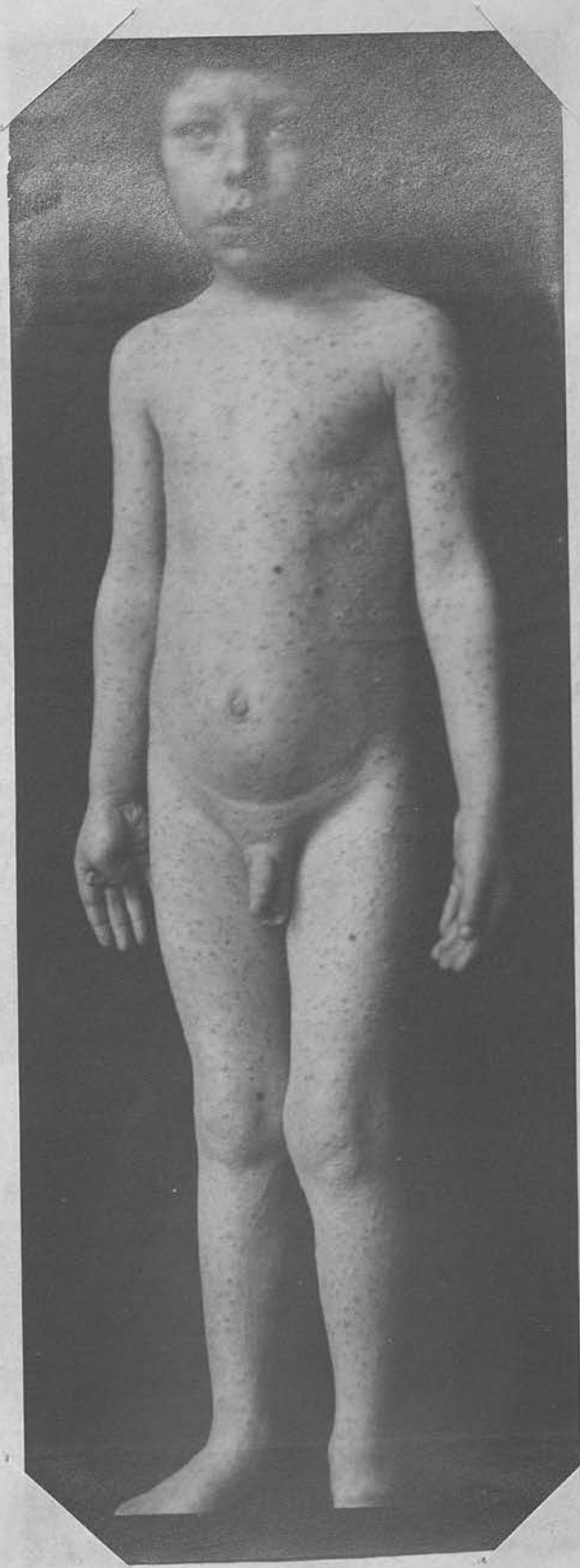
with Smallpox. But in a few only were many lesions to be seen on the extremities, and in the great majority the hands and feet were quite free. In none was the rash more dense on the extremities than on the trunk and in the cases in which the extremities showed a moderately dense rash, decrease in the density with distance from the trunk, with one exception was well marked.

A.B. female, age 7, was admitted shewing a rash of which the great majority of the lesions had desiccated. The minority were in a pustular condition.

The rash was almost uniform in distribution, but, as far as one could judge, the comparative density was in this order, face, trunk and limbs. There were a few lesions on the fore arms and hands and on the legs and feet. It was difficult to form a definite opinion in regard to the distribution of the rash as it affected the limbs but certainly it did not increase in density with distance from the trunk. The patient had been vaccinated in infancy but shewed indifferent scars. No reliable assistance could be obtained from an examination of the crusts. Revaccination was successful. Such is an example of the combination of circumstances in which serious difficulty in the differentiation of Chickenpox may be encountered. It is noteworthy as the one example in a considerable number of selected cases of the disease.



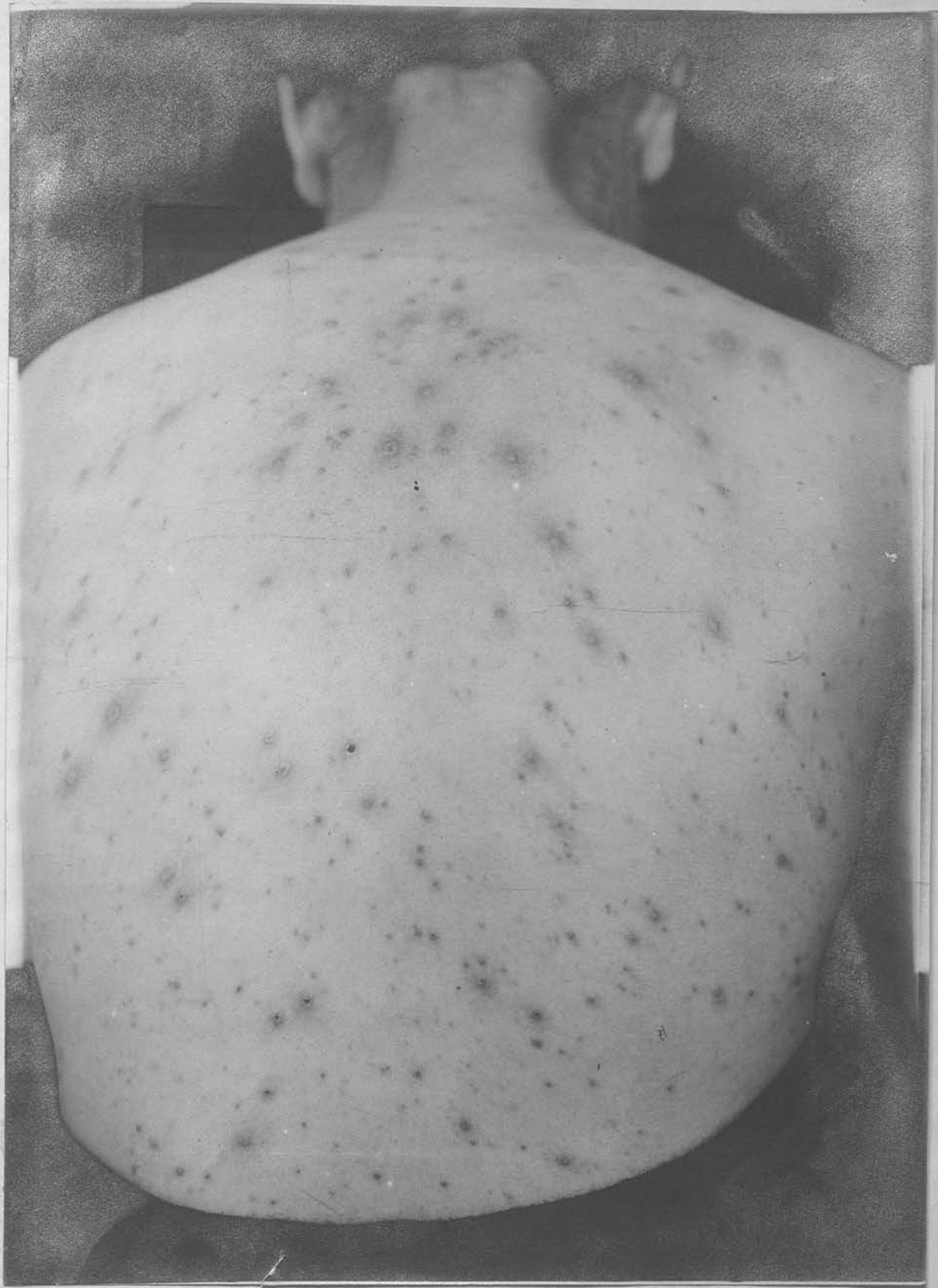
Severe Varicella, shewing typical distribution in that disease.



Very severe Varicella in which the distribution is quite typical of the disease. The hands are free and the feet almost free from eruption.



Varicella, showing characteristic lesions and distribution.



Typical lesions of Varicella in a patient 36 years of age.

Measles

Probably in a certain number of the cases of measles sent to the Receiving Station, the mistaken diagnosis was based on a possible resemblance to the primary reticulate erythema. Reference has already been made to the differentiation of that condition. But in many of the cases received, the diagnosis, as far as one could judge from the condition of the patient on admission, must have referred to the specific eruption in its early stage. In a considerable number of the cases, the patient was an adult. In the majority the disease was of a severe type. In many, the aspect of the face was compatible with the early eruptive stage of the most virulent form of Smallpox. The Grisolie sign in most cases was definite. But in some it was not conclusive and when applied to the rash on the fore-arms and hands, where the lesions were more regularly circular papules it was difficult to form a definite opinion. Koplik's sign was not available in every case. But in none, in my experience, at whatever stage of the eruption the patient was admitted, was the typical Smallpox distribution present. The distinction lay particularly in the distribution of the rash on the extremities. If one assumed from the appearance of the face in several of the patients, that the disease was Smallpox, the comparative density of the rash on the trunk and limbs, and the definite decrease in confluence on the extremities, with distance from the trunk, completely negatived the



A pustular rash shewing a distribution which is quite negative to Smallpox.

assumption. The rash of measles, in my experience, spreads outwards along the extremities as it develops. At any time it is less dense on the limbs than on the trunk and decreases in density with distance from the trunk.

A similar argument may be applied to other papular erythemata, of which several were admitted. In the late stage of the rash, in some cases of Scarlet Fever, the eruption assumes a well marked papular condition on the extremities. But the freedom of the face and the decrease in the density with distance from the trunk was in every case admitted quite a distinctive feature.

One need only refer to Acne, Eczema, Lichen, Herpes Iris, Impetigo, Pemphigus, Scabies, Bromide and Iodide eruptions.

Syphilis In two cases of late pustular Syphilide the lesions were very thickly set on the face, trunk and upper parts of the limbs, but none were seen below the elbow or knee.

There were several examples of the secondary scaly papular eruption. In a few cases such a condition was combined with severe Scabies. The tiny Vesicles about the wrists and fingers presumably were mistaken for the lesions of Smallpox.

Vaccination rashes :- A few recently vaccinated contacts were admitted who shewed a rash consisting of tiny papules or vesicles which at a later stage desiccated



Papular rash with central haemorrhage probably caused by insect bites, shewing a distribution which is negative to Smallpox.

leaving a very small circular crust. But in none of these cases was the face affected and in every case the rash was most densely set on the trunk. No case of auto-inoculated vaccinia was admitted.

Dermatitis due to external irritation (bites of insects etc.) Two sisters were admitted shewing eruptions of the same type and distribution. The rash was discrete and papular and affected the face, neck and upper part of the chest, the back of the hands, forearms, and the dorsum of the feet and ankles. Many of the papules were hard. Some had a surrounding induration. The rash was accompanied by considerable irritation. Many papules shewed a distinct central punctum. Others were capped by a small scale of inspissated serum. The trunk and upper parts of the limbs were almost entirely free from the eruption, which in its distribution had a superficial resemblance to that of Smallpox. The patients had returned from Holland on the day before admission. The rash seemed to be the result of the bites of insects, probably of mosquitos.

In the investigation ^{of the rash} of certified cases of Smallpox at the Receiving Station, the custom was to ascertain first, the Distribution of its lesions, second, the Type or types of its lesions, and third, the inter-relation of its lesions and groups of lesions. But experience shewed that of all differential tests, the

typical distribution was the most reliable, because (1) it is the feature which is most constant in the genuine eruption, (2) it is a feature which is not found in the eruptions most liable to be mistaken for the rash of Smallpox, and (3) it is the feature in the application of which to the suspected rash, the personal factor in observation is most nearly eliminated.